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Special Number on the Internal Secretions – Part I.

INTRODUCTORY.

THE functions of the various endocrinic glands, their influence in health and their responsibilities for disease, is a subject which is daily attaining to an ever increasing importance. The interest attaching to the subject is not only physiological and experimental, but in a very special degree clinical, and it is incumbent upon everyone who practises medicine and surgery to keep himself as far as possible in touch with the progress which is being made in this department. To assist our readers in this direction, we determined to gather into a special number something like an epitome of the present day knowledge of the various questions involved. So vast, however, was the field to be covered that one special number was found to be insufficient, and the material had to be divided into two parts. As will be seen from the contents on the front cover, the February issue will be a continuation of the present one.

The difficulties surrounding the task which we set before us were much increased by the outbreak of the war, and had it not been that a large number of contributors loyally carried out their promises in spite of serious obstacles, the difficulties would have been insuperable. It was intended to include articles from several contributors other than those whose papers now appear, but the exigencies of military service in some cases and the difficulties of communication in others necessitated the abandonment of this project. The articles which we are able to publish nevertheless cover the whole field, and are contributed by acknowledged authorities on the subject with which they deal, and the two numbers may be said to constitute an authoritative pronouncement on what is known of the endocrinic glands and their functions at the present moment.

THE THEORY OF INTERNAL SECRETION: ITS HISTORY AND DEVELOPMENT.

By E. GLEY M.D., LL.D.

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THE idea of internal secretion was propounded first by Claude Bernard and was afterwards developed by Brown-Séquard.

I.—THEORY OF THE DUCTLESS GLANDS.

It must not be supposed that before the time of Claude Bernard the ductless glands were unknown. On the contrary, the distinction between these and other glands was early recognized. In 1845, J. Müller wrote in his celebrated "Manuel de Physiologie:" "The ductless glands are alike in one particular: they either produce a definite change in the blood which circulates through them, or the lymph which they elaborate plays a special rôle in the formation of blood or of chyle. In every instance venous blood and lymph are the only substances which pass from the gland into the general economy."[1] It is noticeable that Müller

[1] J. Müller: *Lehrbuch der Physiologie*, 1844. Translated into French by A. J. L. Jourdan. Paris, J. B. Baillière, 1845. There is a little difference between this purely hypothetical statement and an earlier pronouncement by Burdach: "The vascular or blood glands are agglomerations of vascular ramifications united by the primordial mass, which have neither excretory ducts nor an immediate connection with the mucosa, and which can be concerned only in the metamorphosis of the blood without the agency of an external medium. This metamorphosis may occur as the result of the passage of the blood through the glands, for it is inconceivable that that passage should be unattended by some change in the proportion of the secondary elements; or it may result from nutritional processes within the organs, or from a deposition of substance within their tissues; or it may be due to the formation in the tissues of a liquid which is afterwards resolved." (C. F. Burdach, *Traité de Physiologie considérée comme science d'observation*. Translated into French by A. J. L. Jourdan, Paris, J. B. Baillière, 1837–1841, t. IV., p. 83.) It is evident from this that it is hardly possible to consider Burdach and Müller as the precursors of the theory of internal secretion. The same may be said in regard to Henle, Kölliker, and even more emphatically in regard to Bordeu. (*See* E. Gley: *Relations entre les organes à sécrétions internes et les troubles des ces sécrétions*, Int. Congress of Medicine, London, 1913. Section *Physiology*. Part I., pp. 2–5.)

advances no facts in proof of his assertion. He merely adduces a syllogistic argument, founded upon morphological observation, thus: There are glands which possess no excretory duct; hence venous blood is the only principle which issues from them; therefore this venous blood contains something elaborated by the glands. No experimental facts are brought forward in support of this assertion, and, indeed, after reading Müller's résumé of what was known about the ductless glands in his day, one is impressed, less by the absence of all positive knowledge of the subject, than by the disproportion between the importance attaching to the thesis and the inadequacy of the documentary evidence brought forward in support of it. The literature of the subject consists solely of anatomical findings, hypotheses, and confessions of ignorance; of these, the latter may be regarded as the least detrimental.

The other physiologists of the day are not more illuminating than Müller. How should they be? Like Müller himself, they were unable to furnish a single fact in support of this view, and their conception of the function of the ductless glands was pure hypothesis. It was undoubtedly for this reason that the subject remained for so long sterile. The physiological notion of an internal secretion is indissolubly bound up with the anatomical presentment of a vascular gland, but, before the former can proceed from the latter, one certain proof, at least, of the existence of such an internal secretion must be forthcoming.

II.—THEORY OF INTERNAL SECRETIONS. CLAUDE BERNARD'S NOTION.

This proof was furnished by Claude Bernard, who at the same time definitely associated himself with the doctrine of internal secretion. In 1893 and 1897 I published[1] a collection of evidence which goes to show that, when Claude Bernard demonstrated the formation of glycose by the liver and its presence in the hepatic veins (1855), he immediately recognized the significance of his discovery in its relation to the theory of internal secretion, and that on several occasions he

[1] E. Gley: *Conception et classification physiologiques des glandes* (*Revue scientifique*, 1893, LII., 8–17). *Exposé des données expérimentales sur les corrélations fonctionnelles chez les animaux* (*L'Année biologique*, 1897, I., 313–330). *See also* my *Lecture before the International Medical Congress, London*, pp. 6–8.

drew attention to this aspect of the matter.

Nevertheless, it is a curious thing that for more than twenty years, so far from proving fascinating to the biologist, the theory attracted no attention whatsoever.[1] Physiologist and clinician were alike preoccupied with the glycogenic function of the liver and all its far-reaching consequences. The idea of an internal secretion, as defined with the utmost precision by Claude Bernard, remains unexplored.[2] This indifference is even more astounding when viewed in the light of subsequent events. In 1856, Brown-Séquard described the fatal results consequent upon the extirpation of the supra-renal capsules, and he concluded that these glands supply to the blood issuing from their parenchyma products which are of vital consequence to the organism. In the same year Vulpian demonstrated that the supra-renal venous blood contains the colouring matter which characterises the gland itself. From 1862 onwards, M. Schiff devoted himself to proving that there is a close relationship between the function of the spleen and the proteolytic activity of the pancreas. E. de Cyon in 1870, and W. von Schröder in 1882, established the fact that the urea found in the hepatic veins is the outcome of hepatic activity. M. Schiff in 1859 and again in 1884 described the more striking effects of ablation of the thyroid gland. And, finally, the Swiss surgeons, J. S. Reverdin and A. Reverdin (1882–3) and Kocher (1883), described post-operative myxœdema precisely similar to the spontaneous myxœdema which had already been studied by the English physicians W. Gull (1872) and W. Ord (1878).

How did it come to pass that a mind like Bernard's, as profound and penetrating as it was sagacious, and with a grand

[1] "It is interesting in this connection to note the inequalities of fortune by which scientific ideas are attended. Some, though based on inconclusive findings and hasty deductions, acquire a rapid success. Others, though founded on positive results, are slow to attract and to retain attention, and in this category Claude Bernard's theory belongs." (E. Gley. *Lecture delivered before the International Congress of Medicine, London*, p. 8.)

[2] As far as my knowledge goes, the phrase "internal secretions" was at this period employed only by Charles Robin in his *Leçons sur les Humeurs normales et morbides*, Paris, 1867, p. 239, 2nd edition, 1874, p. 316, and by Paul Bert in an elementary work entitled *Leçons de Zoologie*, Paris, 1881, pp. 248 and 254 (see E. Gley: *Lecture before the International Medical Congress, London*, 1913, p. 9, and *Les sécrétions internes, principes physiologiques, applications à la pathologie*, Paris, J. B. Baillière, 1914, pp. 17–19).

capacity for generalization, failed to perceive the relationship between these discoveries (I refer naturally to those previous to 1878, the year of his death) and the idea of internal secretion ?

I believe myself, and not without a show of reason,[1] that this lack of perception is due to the preconceived idea which Bernard seems to have formed of the nature of the internal secretions. He believed that the ductless glands supplied the blood with its essential constituents and that their purpose was to maintain its composition. It is for this reason no doubt that he was unaware that urea, a substance formed in the liver, is a product of internal secretion. He was merely interested in the destination of this substance, which is not retained in the blood-stream but is eliminated by way of the kidneys.[2] Having allowed E. de Cyon's observations concerning urea to pass him by, he was unable to appreciate those of Brown-Séquard in regard to the effects of epinephrectomy, those of Schiff concerning the effects of thyroidectomy, and the equally interesting discovery of Vulpian. Does it not seem highly probable that, in each instance, the fundamental reason for his blindness was the same—the observations were in no way associated with the composition of the blood, with the building up of the "internal medium," to use his own striking phrase ?

A further question arises. How was it that Schiff, in spite of his talent for observation and his keen, alert intelligence, was unaware of the obvious connection between his own discoveries and Claude Bernard's theory ? That it was so only shows how little notice the theory excited even during the lifetime of its author. Vulpian was the sole physiologist of his day to furnish definite proof that a substance elaborated by a gland passes into the venous blood of that gland. In making this discovery, he defined one of the characteristics essential to the constitution of an endocrinic gland, yet he remained oblivious to the significance of his discovery and failed to pursue the matter further. Suppose for a moment

[1] *See* my *Lecture before the International Medical Congress, London*, 1913, pp. 7, 9, 11.

[2] Such a substance may to-day be defined as an "interno-external secretion." (*See* my *Lecture before the International Medical Congress, London*, 1913, p. 20.)

that this clever and highly experienced scientist, in whom the critical faculty was so developed and so well-balanced, had followed up the line of research thus indicated and had systematically investigated the properties of the blood in the suprarenal veins. If the scanty knowledge of organic chemistry of his day had proved a bar to his researches, the path of experimental physiology was always open to him, and it is along those lines that research to-day is chiefly conducted. We must assume that the idea of a new field for observation simply did not occur to him; the reason doubtless was that, influenced by the theory put forward by Claude Bernard, he conceived the function of the endocrinic glands to be limited to the maintenance of the composition of the blood. Hence, he believed the only problems awaiting solution in this direction to be chemical problems. That physiological activities might reside in the blood which issues from the endocrinic glands, was a possibility outside his field of vision. It may be, too, that he was lacking in that mental courage and experimental audacity, which were present in such a superlative degree in his contemporary and friend, Brown-Séquard.

III.—DEVELOPMENT OF THE THEORY OF INTERNAL SECRETION. BROWN-SÉQUARD'S THEORY.

Between 1889 and 1891, a new element was imported by Brown-Séquard into the accepted notion of internal secretion.

The moment was a propitious one. The morphological conception of the ductless glands was universally accepted. In the department of histology and embryology discoveries had been made, which were destined not only remarkably to extend our knowledge of the texture of these organs, but to reveal as well the constitution of their elements and, more especially, the nature of their secretory cells. Moreover, the notion of the "internal medium" had become classical. It was known that, as the result of certain very diverse functional processes, the composition of this medium remained constant. Among these, renal excretion was rightly held to be one of the most important; important rôles were also assigned to hepatic glycæmia and the ureopoietic activity of the liver.

That all glands without excretory ducts contribute to the blood-plasma some substance which is either essential or expedient to the maintenance of its composition, had already been affirmed by Claude Bernard. The same fact, when repeated without additions by Brown-Séquard, excited universal attention and was acclaimed as a fundamental truth. All that remained was to identify practically all the principles conveyed to the blood by the endocrinic glands.

The achievement of Brown-Séquard lies in this. He assumed that the endocrinic glands supply principles to the blood which have an "elective" action upon certain organs, whether adjacent or removed from them.[1] His assumption suggested "an inter-relationship between the various cells of the economy, effected by a means other than that of the nervous system."[2]

Thus, two entirely new ideas of far-reaching significance were introduced: the idea of specific functional stimulants, substances to which Starling, in 1905, was to give the name of *hormones*; and the idea—physiologically no less important—of functional humoral correlations. These notions, however, were in need of a substantial basis of proof, which was not immediately furnished by their author. For, as I pointed out in 1897, the facts brought forward by Brown-Séquard in support of his theories cannot be regarded as conclusive.[3] Both theories have since, however, received the attention which their originality and fertility demand. To Claude Bernard's idea of the chemical modification of the blood by products supplied by the ductless glands, a second theory was associated, a theory which surpasses the former as the dynamic surpasses the static, that namely of the specific elective action of substances of glandular origin upon different organs and

[1] "These specific soluble products pass into the blood and, by its agency, react upon the cells of other atomic elements of the organism." Brown-Séquard and d'Arsonval: *Recherches sur les extraits liquides retirés des glandes et d'autres parties de l'organisme et sur leur emploi, en injections sous-cutanées, comme méthode thérapeutique. Arch. de Physiol.*, 1891, 5th series, III., 491–506; *see* p. 496.

[2] Brown-Séquard and d'Arsonval, *loc. cit.*, p. 496.

[3] *Loc. cit.* (*L'Année Biologique.* . . . .) Swale Vincent's pronouncement is, perhaps, a little severe. He says: "Much interest was aroused by the work of Brown-Séquard in 1889 upon testicular extracts—work which demonstrated great lack of critical power in its author." (*Internal Secretion and the Ductless*

tissues.

IV.—EXPERIMENTAL GROUNDS UPON WHICH THE THEORY OF INTERNAL SECRETION IS BASED.

In order to establish the new idea of internal secretion upon a sound basis, it was essential that an active principle, the stimulant of an organic function, should be discovered in the venous blood of one or other of the ductless glands. A large amount of evidence was not requisite. The doctrine itself was founded upon the discovery of glycose in the blood of the hepatic veins, and here also a single fact, if incontrovertible, would suffice.

Long before the discovery, however, of a venous blood endowed with physiological properties, the new theory had become widely accepted. Hepatic antithrombine and the anticoagulant property of the liver were not discovered (Gley and Pachon) until 1895 and 1896 (Delezenne), and it was not until the end of 1895 that the even more momentous discovery of the cardio-vascular action of the suprarenal venous blood was made (N. Cybulski, 1895; J. P. Langlois, 1897; A. Biedl, 1898; G. P. Dreyer, 1899). The presence of secretin in the veins

Glands. London, Ed. Arnold, 1912, p. 6). "Brown-Séquard found that subcutaneous injections of extracts of testis exercised considerable influence upon the general health, as well as the muscular power and mental activity . . . It is probable that a good deal of Brown-Séquard's personal benefit under this treatment is to be attributed to suggestion." (*Ibid.*, p. 67.) Yet Swale Vincent himself quotes the ergographic experiments of Zoth and Pregl (1896), in which the authors excluded all sources of error due to suggestion. However that may be, and in spite of the manifest physiological weakness of Brown-Séquard's work, the fact remains that it has proved to be of epoch-making significance. This is partly due to the peculiar interest attaching to the facts which he disclosed, partly to their supposed therapeutic significance, and partly, undoubtedly, to the enthusiasm with which he proclaimed them. It cannot be denied that, from the moment of that pronouncement, the idea of internal secretion took possession of the general imagination, while at the same time the question assumed a totally different aspect. This I have always maintained (lecture before the International Medical Congress, London, 1913; also my *Essais de Philosophie et d'Histoire de la Biologie*. Paris, Masson & Co., 1900, pp. 254–256; also my *Traité élémentaire de Physiologie*. Paris, 1909, p. 1143, 3rd edition, p. 1182), and A. Biedl expresses a similar view in his remarkable work, *Innere Sekretion* (English translation, *The Internal Secretory Organs, their Physiology and Pathology*. London, John Bale and Sons, p. 5). He says: "As the founder of the doctrine of internal secretion, Brown-Séquard has opened to physiology a new and fruitful field for experiment. he has paved the way for the right understanding of many pathological derangements, and he has pointed out a rational and, in many cases, a remarkably successful method of treatment."

of the jejunum was demonstrated by Wertheimer in 1902,[1] and by Fleig in 1903; its presence in the systemic arterial blood was demonstrated by Enriquez and Hallion in the same year. The presence of the pancreatic hormone in the blood which issues from the pancreas was quite recently discovered by Hédon (1911 and 1913), and he further showed that this blood is able to reduce the glycosuria consequent upon extirpation of the pancreas. However important to both physiology and pathology this series of discoveries may be, it cannot be denied that the sum of our knowledge concerning the rôle played by the venous blood of the different glands is very modest. "Although the theory of internal secretion was undergoing a gradual development, the foundation upon which it rested remained very circumscribed. The number of the substances, of the presence of which in the venous blood incontrovertible physiological proof has been obtained, is only four: the pancreatic element which regulates normal glycæmia, hepatic antithrombine, secretin, and adrenalin."[2]

And, in truth, the development of the doctrine of internal secretion did not proceed along the sure and rational lines of logical experiment. It was the outcome of a very simple method, that which Brown-Séquard employed in his investigation of the therapeutic action of testicular extract, and which may be described as "the method by organic extracts." It is not difficult to appreciate the causes which led to this paradoxical situation, in which a sound doctrine was established by the agency of an imperfect method.

As I have already stated, it was not Brown-Séquard's incomplete study of the properties of testicular extract which furnished the experimental basis for his theory concerning the activity of the internal secretions, nor which supplied the impulse for its subsequent development. The sources of this development are to be found in researches at that time undertaken, with the object of determining the nature of thyroid

[1] It should be borne in mind, however, that Wertheimer's experiments were undertaken, not with the normal stimulant of the duodeno-jejunal mucosa, namely hydrochloric acid, but with volatile oil of mustard and with ether, which possess the property of liberating secretin from this mucous membrane.

[2] E. Gley, *Les Sécrétions internes, Principes physiologiques, Applications à la Pathologie.* Paris, J. B. Baillière, 1914, p. 42.

extract and the comparative action of supra-renal extract and supra-renal venous blood.

In 1890–1, G. Vassale in Italy and E. Gley in France showed that animals (rabbits and dogs) which had been deprived of their thyroid could be kept alive by the injection of sufficient quantities of thyroid extract. The application of the method to the treatment of myxœdema immediately followed, and on October 10th, 1891, G. R. Murray published the first case of myxœdema to be cured completely by thyroid medication. From that moment, as everyone knows, the method leaped into favour, for, not only did it constitute a specific treatment for a disease hitherto regarded as incurable, but it was successfully employed in a number of other morbid conditions. Thus, from its early inception the notion of internal secretion passed at one bound into the domain of therapeutics. This brilliant success was due to the immediate application to pathological conditions of the results obtained by experimental physiology, such results on their side being directly influenced by surgical findings—an instance of the advantages to be derived from the closer association of clinical medicine and experimental physiology.

While appreciating to the full the therapeutic value of thyroid extract, it is essential that the biological significance of the facts associated with its action should not be lost sight of. In the first place, definite proof was provided of the value of the glandular extract as a substitute for the gland itself, whether experimentally removed or destroyed by disease. In the second place, a large amount of research was undertaken with the object of elucidating the mechanism by which the extract produces its effect. These experiments revealed and defined within well-marked limits the essential property of the extract, which is to augment the respiratory and nitrogenous changes, the reverse of which obtains in thyroidectomised animals and myxœdematous subjects.[1] The influence

[1] It is obvious, however, that this is insufficient to account for the symptom-complex of myxœdema, and that it sheds no light on the pathogeny of the condition. The reduction in the respiratory changes is purely symptomatic; it may be an outcome of the malady, it cannot be regarded as in any sense a cause of it. "There are causes other than the loss of the thyroid function, which bring about a reduction in the transmutation of matter and which do not give rise to this syndrome; and there are means of promoting nutritive changes which do not effect its disappearance." (E. Gley, "On the

of thyroid extract on the development of the skeleton and the central nervous system (morphogenic influence of the thyroid gland) was also established. Unfortunately, the discovery of iodine in small quantities in the thyroid did not explain, as had been anticipated, either the general functional mechanism of the organ or its influence and that of its extracts upon metabolism. "The significance of iodine is problematic, though the beneficial effects of thyroid substance administered as a drug seem to depend very largely upon its iodine content."[1]

However that may be, all experiments had shown that the function of a gland may temporarily be restored by the exhibition of the extract of that gland, thus justifying all that Brown-Séquard had claimed.[2] Moreover, this was the first example of a combination of concordant facts, physiological, pathological, and therapeutic, uniting to ascribe to a gland the function of internal secretion, at a time when there was no direct proof of the existence of such a secretion. How far may this conclusion be regarded as legitimate? "In cases only where the extirpation of an organ or its destruction by disease gives rise to a symptom-complex, the attenuation or disappearance of which is obtained by the regulated exhibition of the specific organic extract, or by implantation where such is practicable. The success of a substitution therapy is the counter-verification to the results obtained by the destruction of the organ."[3] Thus, in place of the direct proof—that is to say, the chemical and physiological determination of a specific product in the venous blood of a given organ—the doctrine of internal secretion was established by a concordance of indirect evidence. Organo-therapy, so vaunted by Brown-Séquard, received here not only manifest confirmation but stimulus of the most powerful description.

A similar state of things arose in the case of the brilliant discovery by Oliver and Schäfer in 1894 of the cardio-vascular

Pathological Physiology of Myxœdema, lecture delivered before the section of General Pathology and Pathological Anatomy, XIIth International Congress of Medicine, Moscow, 1897.")

[1] Swale Vincent, *loc. cit.*, p. 352.

[2] "The work of Brown-Séquard, in 1889, upon testicular extracts was, perhaps, of doubtful value in itself, but it served to stimulate research in various directions, and led directly or indirectly to very valuable results." (Swale Vincent, *loc. cit.*, p. 23.)

[3] E. Gley: *Lecture before the International Medical Congress*, London, 1913, p. 26.

action of supra-renal extract, a discovery which was energetically followed up both by Schäfer and certain of his pupils, Swale Vincent, Herring, and others. The crucial point in this instance was the demonstration of well-defined physiological properties, manifested by an organic extract in very small quantities, and pointing to the elaboration of an internal secretion by the organ. The inference became a certainty a year later, when it was shown that supra-renal venous blood produces physiological effects precisely similar to those brought about by extract of the medullary portion of the gland. Final proof was afforded when adrenalin, the active principle of the suprarenal, isolated by Takamine (1891) and simultaneously by Aldrich, was detected in the venous blood of the supra-renal capsule. Whether consciously or not, there was a common impulse towards generalization[1] (which, after all, is a human attribute even in the case of the man of science), as well as to the belief that study of the physiological aspects of organic extracts would reveal the specific properties of the internal secretions.

Such, it seems to me, is the sequence of events which has been instrumental in confining the study of the organic extracts almost exclusively to the nature of their therapeutic and physiological activities. This state of things is the outcome of an erroneous method of thought, which is by no means infrequent in experimental science. One aspect of a problem being visualized, other aspects are left out of count. The action of an organic extract may well be an inference of internal secretion, but this inference does not become proof until it is associated with other facts which must be included in one of two categories. Either the extirpation of an organ, from its histology believed to be of glandular nature, must be followed by symptoms which can only result from the loss of a specific active principle, these symptoms disappearing upon the exhibition of that principle in one form or another; or, there must be the direct discovery

[1] "Intravenous injection does not appear to have been much used in the study of internal secretions until the publication by Oliver and Schäfer of the extraordinary effects upon the heart and circulation produced by the injection of adrenal extract . . . . The remarkable discovery of Oliver and Schäfer stimulated numerous observations upon the special physiological effects of extracts made from different organs and tissues." (Swale Vincent, *loc. cit.*, pp. 24 25.)

of an active principle in the venous blood of a gland, such active principle being also characteristic of the secretion of the tissue of the gland. From these two methods there is no appeal. To eschew them is to be removed from the legitimate field of research, where alone positive proof of an internal secretory function is obtainable.

The method by organic extracts is, in its very nature, vitiated by error. At an early date, however, the line of error was detected by more than one physiologist (E. Gley, 1899; Levandowsky, 1899; M. Lambert, 1907; Aldo Patta, 1907; Swale Vincent, 1910), and I have emphasized the facts in a critical exposition of the method in its relation to the question of internal secretion.[1] The fact of a toxic action by the extract of an organ does not justify the assumption of an internal secretion on the part of that organ, for there is no *à priori* proof that the substances present in the extract are normally and regularly excreted in the venous blood of the gland from which the extract was derived. There are, moreover, three groups of experimental facts which militate against the physiological significance ascribed to the action of organic extracts: (*a*) The multiplicity of the extracts possessing a similar physiological action, which tends to prove, not a specific phenomenon, but a pharmacodynamic property. (*b*) The phenomenon of rapid immunization, or tachyphylaxia, from the toxic or physiological effects of many extracts, whilst the action of a true internal secretion, on the other hand, is repeated quasi-indefinitely.[2] (*c*) The necessity of employing certain of the organic extracts in enormous quantities in order to produce a characteristic physiological effect, quantities the weight of which represents the total mass of one or even more specific glands. It is very evident, then, that "the results obtained by pharmacodynamic investigation of the organic extracts supply no proof of the physiological activities of the organs themselves. How can it be sustained that effects obtained by experimental violence are able to supply this proof?"[3]

The mass of research which has been undertaken with the organic extracts has supplied one memorable fact and one

[1] E. Gley, *Lecture delivered before the International Congress of Medicine.* London, 1913, pp. 24–30. *Les Sécrétions internes.* Paris, 1914, pp. 42–54.

[2] The word was coined by Champy and Gley in 1911 (*Comptes-rendus de la Soc. de Biol.*, LXXI., pp. 159, 352, 430).

[3] E. Gley, *Les Sécrétions internes*, p. 54.

only. It seems that, by reason of their physiological properties, certain organic extracts form efficient therapeutic agents. Of these, some are already included in the *materia medica*, where a proportion will doubtless remain. The classic theory of internal secretion will, however, develop along more legitimate physiological lines.

V.—DIRECTION OF FUTURE RESEARCH.

The force of logic is irresistible. It is high time that the exclusive employment of the method by organic extracts should be abandoned, and that research should be conducted[1] on sound physiological lines. In the first place, chemical and physiological proof of the existence of a specific active principle in the tissue as well as in the venous blood of a gland should be forthcoming. In the second, the conditions under which the secretion of such a principle takes place should be determined.

According to a method of classification, which I have described elsewhere,[2] the endocrinic glands with their secretions may be divided into two principal groups: (*a*) the *nutritive* glands (including those which have a morphogenic action, thyroid, hypophysis, thymus), that is to say, which are employed in the transmutation of matter, and (*b*) the *regulatory* and *stimulatory* glands, whose action it is to elaborate hormones.

Of the first group the liver alone has received adequate attention; its glycæmic and ureopoietic functions and the conditions under which glycose and urea, the products of these functions, are eliminated by way of the blood in the hepatic veins have been determined with considerable accuracy. In the case of the morphogenic glands, we have still everything to discover. There is as yet no test which will

[1] This reaction is already in progress. Quite recently, J. Camus and G. Roussy (*La Presse médicale*, July 8th, 1914, pp. 517–521) have expressed themselves concerning pituitary extracts as follows: "It is true that these extracts produce a contraction of the uterus. Seeing, however, that the effect is procurable by extracts obtained from bulls and steers, to deduce from the action of the extract the part played by the normal gland in the living bull or steer, is a somewhat embarrassing problem."

[2] E. Gley, *Classification des glandes à sécrétion interne et des produits qu'elles sécrètent*. *La Presse médicale*, 27th July, 1914, p. 618; and *Les sécrétions internes*. Paris, 1914, pp. 68–72.

enable us to detect, in the venous blood of the thyroid gland, the principle which governs the development of bony tissue and of the central nervous system. The only conclusive test, which would be actually practicable, would consist in the treatment of myxœdematous animals,[1] not with thyroid extract, but by injections of thyroid venous blood. But the technical difficulties by which such a procedure would be surrounded, may be imagined.

In so far as the hormone-producing glands are concerned, there is also wide room for investigation. Although there is justification for the belief that the lacteal secretion is due to a humoral influence, the real source of the galactagogue substance continues to elude us. The two best known hormones are undoubtedly secretin and adrenalin. But in spite of the fact that, as the result of Bayliss and Starling's famous experiments in 1902, certain of the conditions governing the production of secretin are now determined, we do not yet know with any degree of certainty, whether or no this substance is present in the intestinal mucous membrane intact, and is simply extracted by the so-called excito-secretory agents which are, in reality, merely solvents.

The best methods of research are those by which the discovery of adrenalin was effected. When our knowledge of the principles secreted by the thyroid and the other ductless glands, is as advanced as our knowledge concerning the principle of the suprarenal, the doctrine of internal secretion will have made a decisive step forward.

[1] It is easy to obtain rabbits which present cutaneous trophic disturbances and a general condition reminiscent of myxœdema (E. Gley).

THE PHYSIOLOGY OF THE THYROID GLAND.

By H. H. DALE, M.A., M.D., F.R.S.

SETTING aside the random guesses of earlier writers, we obtain the first clear evidence on the function of the thyroid gland, as on that of the supra-renal capsule, from clinical and *post-mortem* observation in England. Cretinism and myxœdema, and their relation to thyroid defect, will be dealt with elsewhere in this Special Number of THE PRACTITIONER. Here it may be noted that the association was first experimentally verified, and the relation of cause and effect made definite beyond question, by the experience of surgeons in Switzerland on the sequelæ of removal of the thyroid for goitre.

A review of the extensive records of extirpation experiments on the lower animals, gives an impression which, at first sight, differs considerably from that gathered from observations on the human subject. Occasionally a prolonged cachexia is recorded, with points of resemblance to myxœdema, and Horsley succeeded in producing what he regarded as true myxœdema, by removal of the thyroid in adult monkeys. On the whole, however, the results of thyroid extirpation in the lower animals appeared, in comparison with those in man, either surprisingly small, or surprisingly acute; there resulted either a vague and mild cachexia, often detected with difficulty, or an acute condition of nervous excitability, with muscular rigidity, tetany and rapidly fatal termination. This "post-operative tetany" had occasionally been seen to follow thyroid removal in man, though less commonly than "post-operative myxœdema." Since fatal tetany was the usual result in carnivora, while the results in adult herbivora were habitually slight and often imperceptible, it was natural to attribute the difference to diet, especially as a pure meat diet was found to accelerate and aggravate the nervous symptoms produced in dogs.

The matter was placed in a new light when Gley discovered the significance of the parathyroids, and showed

that these bodies (in reality only one pair of them, now usually known as the "external parathyroids") were so differently situated, in the different species, as to be habitually left behind when the thyroid was removed from herbivora, and as regularly removed with the thyroid in the operation as ordinarily performed in carnivora. He found that, when the operations in the different species were made really equivalent, the difference in result vanished. Then Vasale and Generali, and many subsequent observers, found that removal of all the parathyroids alone, with preservation of the thyroid, caused tetany. So that the influence of diet and species fell into the background, and the view became prevalent, and remains so, which regards the acute nervous symptoms as due entirely to parathyroid removal, or injury; the effect of simple thyroid removal being, in the young, a stunted idiocy, analogous to cretinism in man; in the adult, a cachexia having, at least, something in common with myxœdema.

According to this view the thyroid and the parathyroids are independent, and even to some extent antagonistic, in function; and its acceptance is implicit in the editorial plan, which allots parathyroid physiology to a separate article. Here, then, we are concerned with what, on this hypothesis, is certainly known of the function of the thyroid proper. In the first place, however, it is desirable, while admitting that this theory of independent parathyroid function is supported by the greater volume of evidence at present available, to consider certain indications of an opposite tendency. For though, as a working hypothesis, and a basis of presentation, the view is admissible, it cannot be regarded as proved beyond discussion.

A good deal turns on the technical difficulties experienced in removing the parathyroids completely, and there are not wanting those who maintain that it is impossible to do so, without causing such extensive injury to the thyroid, that the latter is left seriously inadequate. The contention is hardly convincing, since it is admitted by all that complete removal of the thyroid does not cause tetany, provided a pair of parathyroids be left *in situ* or even successfully grafted elsewhere.

There are other more serious difficulties, however. When

the thyroid is removed, the remaining parathyroids hypertrophy, and may develop vesicles, containing a substance, which at least resembles colloid in microscopic section. It is stated, further, by some, that the intervesicular tissue of the normal thyroid contains groups of cells microscopically indistinguishable from parathyroid tissue. Such authors, therefore—the most prominent being Vincent and his co-workers—incline to return to Gley's original view of the parathyroids, as partly developed, and potentially functional nodules of thyroid tissue. In further support of this view may be quoted the fact, admitted even by the convinced advocates of separate function, that post-operative tetany in man is greatly benefited by administering thyroid substance. The sheep's thyroid generally used contains, indeed, the substance of the internal parathyroids; but pure parathyroid substance, in far larger amounts, has not the remedial action. Clearly the last word on the relation of these structures has not been said; and, with that reservation, we proceed to consider the thyroid separately.

EFFECTS OF THYROID DEFICIENCY.

In mammals, other than man, the effects of extirpating the thyroid, with preservation of at least one pair of parathyroids, are much more marked in the young than in the adult subject. In the young of various species a cretinoid condition results, with slow growth, delayed ossification of epiphyses, small development of the face in relation to the rest of the skull, protuberant abdomen, and sexual infantilism. In some species the hair growth is scanty, in others abnormally long and coarse. An interesting observation is that of extensive atheromatous degeneration of the aorta, found *post mortem*, and recalling the resemblance, indicated by Horsley, between some of the results of thyroid deficiency and those of senile decay.

In both young and older animals thyroid removal produces a marked depression of metabolism—a retardation of vital functions in general. The most noteworthy effect is on protein metabolism, nitrogenous excretion being greatly reduced, and the need for protein food correspondingly diminished. Fat metabolism suffers a like reduction; the tendency to obesity is a familiar result of relative thyroid deficiency. On the other hand, the capacity for using carbohydrate would seem to

be increased, for the thyroidless animal is said to tolerate unusually large quantities of dextrose, without showing glycosuria. Similarly, it is stated that injections of adrenalin less readily produce glycosuria when the thyroid is absent. The respiratory exchange is diminished with the rest of the metabolism, but the depressed appetite and lethargic habit of the animals obscure the significance of the observation. Naturally the reduced metabolism involves diminished heat-production.

A diminished sensitiveness of the sympathetic nerves is described as a result of thyroid extirpation, and figures in a suggested complex scheme of interaction between different ductless glands, of which mention will be made later. Others have pointed out that other autonomic nerves similarly lose sensitiveness when the thyroid is removed. In the same way, while some have described a specific loss of sensitiveness to adrenaline, others state that pilocarpine likewise acts less powerfully than in the normal animal, while atropine dilates the pupil with abnormal ease. A depression of responsiveness seems, indeed, to affect all the excitable tissues.

Anæmia, due to diminished number of the red corpuscles, with a relative increase of mononuclear leucocytes, is a constant feature of the condition following thyroid extirpation. Whether this indicates a direct relation between thyroid function and the hæmatopoietic system is not clear; probably it is merely a feature of the general cachexia. The cachexia in turn may be related to the retardation, which the functions of digestion and assimilation suffer, in common with all other vital activities.

EFFECTS OF THYROID EXCESS.

These are in almost all points the direct antithesis of those resulting from thyroid defect. They may be studied in cases of Graves' disease, or by observing the effects of excessive administration of thyroid substance. For it is a point of great significance in thyroid physiology, that defect of thyroid secretion can be replaced, or excessive activity simulated, by injecting extracts of the gland or administering its substance by the mouth. Of no other ductless gland is this true in equal degree.

The extreme nervous excitability, sleeplessness, tachycardia, reactive vasomotor system, and accelerated metabolism, seen

in Graves's disease, present a very complete contrast with the results of thyroid deficiency, and have all been recorded, though not with any regularity, as resulting from administration of thyroid substance to animals. Even the characteristic exophthalmos has occasionally been so produced. The most constant effect of such administration is accelerated metabolism, causing a marked increase of nitrogenous output, and, if the treatment is continued, rapid emaciation. The respiratory exchange is increased, and the tolerance for dextrose lowered, so that glycosuria often occurs.

It may be noted that wasting results from both thyroid deficiency and thyroid excess, but for apparently opposite reasons. In the former case digestion and absorption are at fault, and metabolism is diminished; in the latter case the metabolic breakdown is unduly rapid.

While the excitability of the nervous system in general is raised, the prominence of certain symptoms of thyroid excess have naturally focussed attention on the true sympathetic system; widening of the palpebral fissure, protrusion of the eyeball, and accelerated heart-beat can all be produced by stimulating the upper end of the sympathetic ganglionic chain. The sensitiveness to adrenalin, again, which so accurately reproduces in its action the effects of true sympathetic nerves, is said to be increased by excessive thyroid activity. Thus Loewi states that instillation of adrenalin into the conjunctival sac, which is without effect on the pupil in the normal subject, causes dilatation of the pupil in the sufferer from Graves's disease. Asher and Flack have found, that the pressor response to a given submaximal injection of adrenalin, in the anæsthetised rabbit, is increased by injecting thyroid extract. But the nervous symptoms of Graves's disease, or those of experimentally produced thyroid excess, are certainly not those of pure sympathetic stimulation; nor are by any means all effects of sympathetic nerves represented in the picture. The most that can properly be claimed on behalf of the suggested specific relation of the thyroid to sympathetic excitability, is that certain of the prominent symptoms of thyroid excess—exophthalmos, tachycardia, the tendency to glycosuria—have a suggestive relation to actions of the sympathetic nerves, or of adrenalin. It may be noted that an

attempt has been made to differentiate two types of Graves's disease, in which super-excitability of the true sympathetic and of the rest of the autonomic system respectively predominate. Two corresponding hormones have even been postulated in the thyroid secretion.

MODE OF ACTION OF THE THYROID GLAND.

Between the rival theories of action which have been advocated, at one time or another, for several of the ductless glands—destruction of naturally arising toxic products, or the production of a secretion necessary for the normal function of other tissues—it is easier to choose in the case of the thyroid gland than in any other. The possibility of replacing an absent or defective thyroid, by administering extracts from, or the substance of thyroid gland, is conclusive in favour of an internal secretion. This does not necessarily exclude the alternative theory of toxin-neutralization; it is still possible to suppose that the secretion of the thyroid acts by neutralizing the effect of substances which, in its absence, produce toxic symptoms. There is, however, but scanty evidence in favour of such a view. The observations on the aggravation, by meat diet, of symptoms following extirpation, come from the period when the significance of the parathyroids was not recognised. Clearly in its favour would be the supposed action of serum or milk from thyroidless animals, in mitigating or removing the symptoms of Graves's disease, if that action were supported by convincing evidence. Probably that evidence will be discussed elsewhere in this number.

A comparatively recent revival of the auto-intoxication theory lays stress on the presence of iodine in the thyroid gland. It is suggested that albuminoid substances, with toxic action, are absorbed from the alimentary canal, and that they are rendered non-toxic in the thyroid by iodization. Here again, the possibility of replacing the action of the gland, by administering extracts or substance, shows that the suggested iodization, if it occurs, can be carried out by substances derived from the thyroid, and does not require the structural integrity of the gland itself. The theory is, in any case, little more than a speculation.

Hunt's interesting observation on the increased resistance

to acetonitrile, which mice acquire by ingesting thyroid substance, has been quoted as evidence of a neutralizing action on toxic substances. This is a misreading of the observation, which, as Hunt and his colleagues showed, applies only to a particular poison and a particular species. To some other poisons the mouse's resistance is lowered by thyroid feeding.

The real value of Hunt's observation is in providing a test for some constituent of the thyroid; though it is not conclusively proved that the constituent so detected is the physiologically important active principle. The test enabled him to obtain further evidence in favour of an internal secretion by the thyroid, and of an excess of such secretion in Graves's disease. He found that blood from those suffering from this condition raised the resistance of mice to acetonitrile, while that from other subjects had no such effect. It may be taken as demonstrated, therefore, that the thyroid furnishes an internal secretion, or hormone, which is essential to normal growth and metabolism, and which has a pronounced action on nervous function.

On the method of the secretion, and the chemical nature of the active constituent, evidence is scanty as yet. One point which stands out clearly, is the peculiar power of the thyroid, among ductless glands, for storing its active principle. In no other case can absence or atrophy of the gland be replaced, with a like perfection and completeness, by administering the gland substance. It is natural in these circumstances, to identify the peculiar colloid substance, filling the vesicles of the gland, as the stored active material. There is histological evidence that this viscid substance arises as droplets in the epithelial cells lining the vesicles. Appearances have also been described, suggesting the passage of colloid between the epithelial cells of the vesicles, or by rupture of the latter, into the lymphatics. There are certain considerations, however, connected with the chemistry of the substance, which may well give rise to doubt as to whether the active constituent enters the circulation in this form.

The most remarkable feature of the chemistry is the presence of iodine in considerable amount, 0·2 per cent. or more being found in the dried gland substance of the sheep.

The iodine seems to be attached to a protein, with physical properties resembling those of the nucleo-albumines (thyreo-globulin of Oswald). The physiological significance of this iodine is far more difficult to determine. Its proportion varies within wide limits in normal animals, in accordance with the iodine content of the diet. In young animals, in which the activity of the thyroid is of the highest importance, the gland contains little or no iodine. This could be interpreted as indicating that the iodine has no relation to the hormone, or, on the other hand, might conceivably be due to the rapid use of the hormone, with practically no storage, in the young subject. Hunt found that such young thyroids had some efficiency in raising resistance to acetonitrile, but that activity in this direction ran, on the whole, roughly parallel to iodine-content. In adult animals no evidence exists showing that thyroid activity becomes excessive when the gland is enriched in iodine by administering iodides, etc., or deficient when the gland is depleted of iodine, by keeping on iodine-free diet.

Various attempts have been made to identify the iodine-containing complex in the peculiar protein of the thyroid. Baumann, by a somewhat severe hydrolysis with 10 per cent. sulphuric acid, obtained a dark, tarry substance, soluble in alkalies, and containing over 9 per cent. of iodine. For this substance, named thyro-iodine, several observers have claimed therapeutic action in conditions of thyroid deficiency and in goitre. The evidence, however, is not perfectly convincing; various artificial iodised proteins, and even fatty acids, have been found to ameliorate symptoms following thyroid deprivation, and iodine itself seems to have some value in reducing goitres.

While it may be doubted whether this drastic hydrolysis yields the true active principle, there is no doubt that the activity of thyroid substance is relatively resistant to such hydrolytic cleavage as occurs in the alimentary canal. The value of administering thyroid substance by the mouth is proof of this. It is quite out of keeping with what is known of protein metabolism, to suppose that a complex protein from a different species can be absorbed and used unchanged; and it is established that the residue left after peptic digestion of thyroid protein is still active. Now it does not seem

probable, when this active residue is absorbed by a thyroidless patient or animal, that it is synthesized into colloid before acting, in the absence of the organ by which colloid is produced. It may be a grouping which readily becomes attached to proteins, and may be distributed in some form of combination with the blood proteins. If that were known to be the case, it might be suggested that the function of the colloid was to anchor such of the active principle as was in excess of immediate needs. But the possibility of such free speculation is a sufficient index of poverty in positive evidence, and of the need for further investigation.

The immediate effects of injecting thyroid extracts into the circulation present nothing characteristic. A fall of blood pressure has been described by some, an increased activity of the heart by others. But either effect, in the degree described, can be produced by injecting extracts from one organ or another, to which no specific function of internal secretion can be attributed.

Asher and Flack described effects of a more suggestive kind. They found that either by injecting thyroid extracts, or by stimulating the nerves supplying the gland, in anæsthetized rabbits, they obtained an augmented response to a stimulus of given strength and duration, applied to the depressor nerve, or to injection of a constant dose of adrenalin. The observation is obviously in line with what is known of the effects of chronic thyroid excess. On the other hand, the apparent indication, that the output of thyroid secretion is under control of the central nervous system through the laryngeal nerves, was hardly to be anticipated from the other known facts of thyroid physiology. These suggest rather the slow, persistent influence of a continuous output, than the sudden gushes of secretion, in response to a rapidly fluctuating demand, such as one associates with nervous control.

The mention again of the influence of thyroid secretion on the action of adrenalin, brings us to the question of the relation between the different ductless glands. There is no section of physiology which offers such temptation to the speculative theorist as this. There is great wealth of suggestive facts, but an almost equal poverty of clearly significant ones. There is room in such a field for wide difference of opinion. There are indications of some relation between the activity of

the thyroid and that of the sex-glands, especially in the female. The swelling of the thyroid at the menstrual period, after defloration, and during pregnancy ; the much greater frequency of Graves's disease in the female than in the male, and its predominant incidence between puberty and the climacteric ; the sexual infantilism resulting from thyroid atrophy or removal in early life ; the disorders of menstruation, associated with either thyroid deficiency or excess—these and many other observations indicate a relation between thyroid and ovarian activity. But it is difficult to give a precise definition of the relation, or to form a clear conception of the mode of interaction. The existence of the relation is as obvious as, say, that between the supra-renal cortex and sexual development and activity in the male, and the meaning, as yet, equally obscure.

In the case of the pituitary gland there is some evidence of an attempt at vicarious function. Hypertrophy after thyroid extirpation has been described, and the formation of colloid. There is no evidence, however, that these changes are effective in replacing thyroid function. The relation of thyroid activity to carbohydrate metabolism, to which allusion has already been made, has naturally provoked the suggestion of an antagonism between the action of this gland and that of the pancreas in this direction. Indeed, a complete scheme has been put forward, in which the actions of the thyroid, pituitary, parathyroid, and supra-renal glands, and of the pancreas, are linked in a complex series of augmentor and antagonistic influences. For any one of the alleged interactions some evidence can be presented. But, at the present stage of investigation, any such precise scheme involves a process of selecting what is apposite, and ignoring or slurring over what is inconvenient. My own feeling is, that the brilliant and suggestive speculations of the Viennese school, in particular, unduly weaken the connection between the thyroid and the parathyroids, and present with undue emphasis and precision its relation to the other ductless glands.

Recent collections of references to the enormous literature of the thyroid gland are to be found in Biedl's "Innere Sekretion," and in Swale Vincent's article in the *Ergebnisse der Physiologie* for 1911.

THYROID INSUFFICIENCY.

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[With Plates I.–XXVI.]

THE subject of internal secretion is one to which a wide interest attaches, and the problems by which it is surrounded constitute a profound preoccupation of modern medical science. Up to now the place of honour has been held by the thyroid gland. The insufficiencies of this organ supply a rich field of observation, and close study is rewarded by results having a very definite clinical significance.

Unfortunately, however, practical acquaintance, even of the most elementary description, with thyroid and pituitary insufficiency is rare. It is my daily lot to encounter physicians possessing only the most superficial knowledge of the subject. These men employ thyroid extract as a drug like any other drug, without knowing why. In the medical journals which they affect, they have met with isolated accounts of its action in some case of chronic rheumatism, asthma, profuse hæmorrhagic or obstinate cephalic affection, and they exhibit the drug on the happy chance of achieving a similar effect. When asked whether they have found traces of subthyroidism among the ascendants or collaterals of their patient, they will not know how to answer. They may even end by admitting that subthyroidism, as a morbid entity, is unknown to them. They no more know why the exhibition of thyroid extract should be followed by abatement of the specific symptoms, than they know why antipyrin relieves headache and trional induces sleep ; what is more, they do not care.

To the better informed, the dosage proves a formidable stumbling-block. There are those who, alarmed by the untoward cardiac symptoms wrongly attributed to the action of thyroid extract, administer the drug in doses so small as to produce results which are inappreciable. Others again risk quantities which are dangerously in excess of the mean, with the result that symptoms of a disquieting nature are provoked. The weight of the body falls rapidly and considerably, there

is alarming palpitation, and the muscular pain and occipital and dental neuralgia, which it was the object of the treatment to relieve, become very much intensified.

In some instances, excessive dosage brings about a rise in temperature, the hypothermia so characteristic of the subthyroidic subject giving place to hyperthermia. This constitutes an incontestible proof of thyroid intoxication. Certain authors, observing the subthyroidic condition pass within a few hours into a condition of apparent hyperthyroidism, have assumed an instability on the part of the thyroid gland. This notion has served still further to confuse the ideas of the practitioner. Later on, I shall offer an explanation of this deceptive symptom, showing how readily it may be explained, and how easily prevented.

It is obvious that myxœdematous dwarfism and infantile cretinism cannot escape detection by a physician of even moderate attainments. But with adult myxœdema, even when of a pronounced type, this is by no means always the case. More often than not, the condition is mistaken for Bright's disease, a degree of plausibility being lent to this diagnosis by the fact that albuminuria is frequently present, and that the cerebral symptoms of myxœdema, namely, giddiness, a dazed sensation, fainting, and coma, are very similar to the symptoms of uræmic origin observed in chronic nephritis.

The slighter forms of thyroid inadequacy are almost invariably missed; yet, owing to their extreme prevalence, the recognition of these is particularly important. We examine our patients, with tuberculosis, syphilis, and chronic alcoholism in view, and we take careful note of consanguinity. But this is not enough. We ought to ascertain the thyroid resources of the patient as well. The conditions governing nutrition and combustion, the rapidity of the organic changes, the probable resistance to infective agents,—these are points with which we ought to concern ourselves. A little later on it will be shown how easy, almost mathematical, research of this nature is.

It is the object of this article to throw some light upon the nature of thyroid insufficiency, using the term in its broadest sense. It is proposed to describe not only severe conditions, the significance of which is apparent at a first glance, but also to define the symptomatic outline of the slighter forms.

It has been said that no one who has once seen a case of true myxœdema, in other words, complete thyroid suppression, could fail to recognize it again. This is quite true. It is my intention to show here as many such cases as the scope of this article and the kindness of the Controlling Editor of THE PRACTITIONER permit.

PHYSIOLOGY OF THE THYROID GLAND.

Having once determined the part played by the thyroid gland in the normal economy, it should be possible accurately to define the symptoms which would result from diminution of its secretion in varying degree. Unfortunately, however, that is a point at which we have not as yet arrived. In the region of established fact all that we can affirm with certitude is: (*a*) that the thyroid governs the building-up of the cells, that is to say, the formation and growth of the tissues; and (*b*) that it regulates the destruction of the albumen molecule, and governs the processes by which waste material, resulting from the incessant regeneration of the organs, is eliminated.

CELL-GROWTH.

No cell, whatever its nature, attains the morphological completeness necessary to the perfect accomplishment of its function, unless it be supplied with a certain essential quantity of thyroid secretion.

The demonstration of this fact is easy. A child suffering from marked thyroid insufficiency, whether spontaneous or as the result of the operative removal of the major portion of the gland, ceases to grow. If he is given extract obtained from the thyroids of sheep, he will begin to grow again. If this treatment is suspended there is once more arrest of growth. Thyroid secretion is essential to the growth of each cell, and it is therefore indispensable to the general development of the individual. This is well illustrated by the following histories of cases:—

Emile L. (Fig. 1, Plate I.) was 20 years of age when I first saw him. According to his mother, he ceased growing at the age of 7. His height was 3 feet 10½ inches. His condition was one of hereditary thyroid degeneracy of tubercular origin, his father having died of pulmonary tuberculosis a few days before his birth. In spite of the small size of the

photograph, the puffiness of the face, the rickety curve of the tibias, the protruding abdomen, and the general infiltration over the entire body are readily discernible. Thyroid extract was exhibited, and there was a resumption of growth; changes took place in the genitals, and at the end of six months they had assumed their normal development. Some authors are of the opinion that the arrest of growth in these cases in due to testicular insufficiency, and they describe the condition as one of "dwarfism due to sexual insufficiency." As a matter of fact, both the arrest of growth and the infantile condition of the genitals are derived from the same source, namely, thyroid insufficiency pure and simple. That this is the case is proved by the success of thyroid medication.

Emile underwent continuous treatment for 5 years. In 1895, his height was 3 feet 10½ inches; in 1900, it was 4 feet 10½ inches, a total gain of 12 inches. In 1900, treatment was suspended.

I saw him again in 1907 (Figs. 2 and 3, Plate I.). In spite of the fact that his physical and mental development were good, I noticed a certain regression, a return to the infantile, more especially in the sexual characteristics. This shows very clearly that the thyroid gland controls, not only the development of the sexual system, but also its trophic maintenance and physiological function. I also remarked an extraordinary relaxation of the rotular ligaments. Dislocation of the patella occurred spontaneously and very readily. It invariably happened on sitting down, and was quite painless (Fig. 3, Plate I.).

The relaxation of articular ligaments is frequently observed in children of arrested growth, who are under treatment with thyroid extract. The ligaments at the internal aspect of the knee-joints are those most frequently affected, with the result that a certain amount of knock-knee becomes apparent. The parents are alarmed by the untoward symptom, and, unless reassured, suspend the treatment. The deformity is corrected, however, as the child grows older. Relaxation of the plantar ligaments in subthyroidic subjects is a frequent source of flat-foot. The pain in the tarsus and the heel, which is sometimes complained of by adolescents, corresponds with a certain degree of thyroid insufficiency. The articulations of the thumb and fingers may also undergo abnormal relaxation,

and it is frequently possible to bend the fingers backwards, until they touch the back of the hand. When gloved, the soft and infiltrated hand loses its form, and, on being squeezed, conveys the impression of a glove filled with clay. It is possible with very little practice to judge of the degree of thyroid inadequacy merely by squeezing the patient's hand.

The following is an example of resumption of growth in a child, suffering from pronounced thyroid inadequacy with arrested development.

A glance at Fig. 4 (Plate II.) is sufficient to show that we have to do here with a case of severe myxœdema, which is revealed by the infiltration of the face and of the entire body. Attention is drawn to the effect of the treatment upon the very marked umbilical hernia, which went beyond the upper margin of the fibrous ring. Under the treatment, puberty supervened. At the end of the first year the abdomen was still very large; by the end of the second year, the cure was complete. The muscular structure was entirely regenerated, and had acquired sufficient strength in the abdominal region to counteract the pressure of the visceral organs.

The next case also illustrates very clearly the constructive properties of the thyroid secretion. When first I saw this child, Fig. 5 (Plate II.), he was 10½. His height was 36½ inches, the height of a boy of 4½. Later on, when discussing the causes of severe thyroid inadequacy, the reasons for his condition will appear.

The infiltration characteristic of thyroid insufficiency is seen to even better advantage in this case than in the preceding one. The heavy, puffy face, the protruding abdomen, the infiltrated limbs, and the rickety crookedness of the legs are all pathognomonic. At the end of the first year the height was 3 feet 6⅝ inches; at the end of the second it was 3 feet 10⅜ inches; and at the end of the third it was 4 feet 2 inches, the total gain being 13½ inches. The intellect, which had been vague and obtuse, gradually developed. The child was sent to school, where he distinguished himself by his application.

The child D. E., whose photograph is reproduced, is the youngest of a large family of normal children. He was born a cretin, and his mother died of pulmonary tuberculosis a few days after his birth. The condition is that of thyroid degeneracy of tubercular origin.

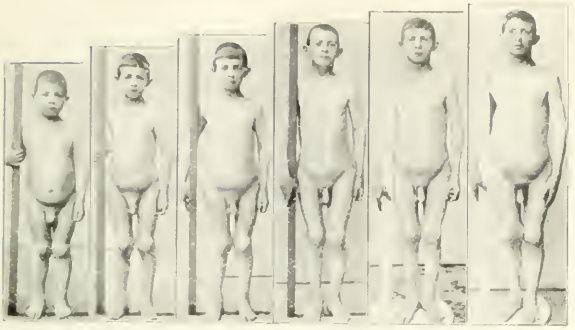


Fig. 1.—Emilie L. Influence of thyroid extract upon the growth of a myxœdematous dwarf. Successive stages, from 1895–1900, showing general improvement and resumption of growth.

Fig. 2.—Emilie L. in 1900.

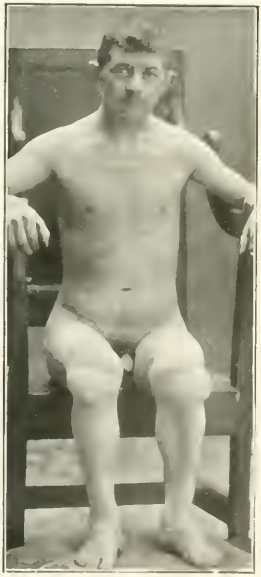


Fig. 3.—The same. Relaxation of the articular ligaments. Spontaneous dislocation of the patellas.

Fig. 4.—*Pronounced thyroid inadequacy in a girl of 18. Arrest of growth. Influence of artificial thyroid stimulation. In 2 years the height increased from* 3 ft. 5½ in. *(height of a child of 8) to* 4 ft. 4 in. *Total gain,* 11 in.

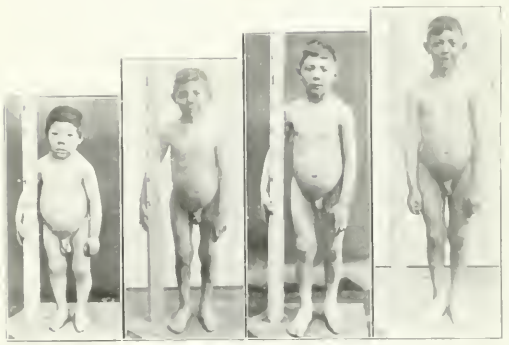


Fig. 5.—*True myxœdema. Age* 11. *Height* 3 ft. 1 in. *Effects of thyroid extract on the growth. Growth at the end of* 1, 2, *and* 3 *years.*

Fig. 6.—*D. E. True myxœdema. Age* 14; *height* 29 *in.*; *protruding abdomen*; *obstinate constipation*; *umbilical hernia.*

Fig. 7.—*D. E. After* 69 *days' treatment with thyroid extract. He has gained nearly* 4 *in. in height.*

Fig. 8.—D[illegible] at the end of 2 years and 9 months' treatment. The abdomen is normal. The umbilical hernia has disappeared; the weight has increased [illegible] pounds.

Fig. 9.—*D. E. After 12 years of treatment with thyroid extract.*

Fig. 10.—*Same as* Fig. 9. *Exaggerated lumbar curve due to relaxation of the ligaments of the spine.*

Fig. 11. [illegible] aged 8, arrest of growth height [illegible] ft. 11 in. instead of 3 ft. 5 in. in normal; protrusion of the abdomen. Results of thyroid treatment after 8 months.

At the age of 14 years (Fig. 6), his height is 29 in., the height of a baby of 18 months. The infiltration of the entire body, the gaping mouth from which the over-large tongue protrudes, the bent tibias, the enormous protrusion of the abdomen, the umbilical hernia, the scanty hair, all these signs point to but one diagnostic conclusion, namely, subthyroidic cretinism in its most extreme form. The intelligence is nil; the expression of his emotions by a few grunts is as much as he is able to accomplish. He is invincibly constipated, and is unable to control his urine either by day or night.

Now see him (Fig. 7) after a 69 days' treatment with thyroid extract. He has grown nearly 4 inches; the abdomen is markedly reduced in size; the infiltration of the limbs is noticeably diminished; and the facial expression has become interrogative and intelligent.

The treatment has now (Fig. 8) been maintained for two years and nine months, and in that time he has grown 16 inches. His intelligence has rapidly developed; he can now speak and takes an interest in everything that goes on around him.

Here he is (Figs. 9 and 10) at the end of 12 years of treatment. His height has increased by 27½ inches; the expression of the face is intelligent; the sexual organs are perfectly developed. Note the exaggerated lumbar curve (Figs. 9 and 10), due to relaxation of the dorsal ligaments. I have observed this sign in other subjects after prolonged treatment with thyroid extract.

So much having been done for this boy, who at the age of 14 measured only 29 inches (9 inches more than a newly born infant) and who represented a complete type of cretinism, how brilliant might not be the results of thyroid medication in the case of children less profoundly affected! That such an assumption is justified is shown by the following history:—

The little girl, depicted in Fig. 11, is 7 years old. Her abdomen is enormous; there is constipation of the most obstinate kind, which frequently terminates in a fit of violent diarrhœa. The face is intelligent and speech is clear. Her neck is short, and the tibias show the syphilitic curve. Her height is 2 feet 11 inches, in place of the normal 3 feet 7½ inches.

Now observe the results of treatment with thyroid (Fig. 11). In 8 months her height has increased from

2 ft. 11 in. to 3 ft. 7½ in.; the abdomen has subsided; and the neck has emerged. This protrusion of the abdomen in children is frequently mistaken for mesenteric tuberculosis (tabes mesenterica).

The following is an instance of slight thyroid insufficiency. At a first glance, this boy (Fig. 12), whose age is 11½ years, does not suggest an impoverished thyroid. He is simply small for his age, his height being 4 ft. 3⅜ in. instead of the normal 4 ft. 6 in.

This child is the victim of generalized alopecia; he is an infantile subject of the Lorain type. His limbs are thin, slender, and fragile; the thorax is elongated and contracted; the ears stand away from the head; the arms are extraordinarily thin and frail. He makes a fairly good figure in his clothes, and it might not have occurred to me to photograph him naked, if former experience had not shown me that hairless children frequently present unequivocal symptoms of infantilism.

The effects of thyroid medication were, briefly, as follows: At the end of six months the patient had gained 1⅓ in. in height, and his hair was growing strongly. At the end of 9 months his height had increased by 1¾ inches, and his hair was normal.

By comparing the profile in the first photograph with that in the last (Fig. 13), it will be seen how the face has gained in intelligence. In the latter picture, the puerile, almost infantile, character has entirely disappeared.

The next portrait, that of the patient's mother, may come somewhat as a surprise (Fig. 14, Plate VIII.). I feel confident, however, that whenever confronted with a child suspected of subthyroidism, whether severe or benign, it is highly expedient to see the mother and, if possible, to examine her. She will frequently be found to show the stigmata of thyroid inadequacy.

In the present instance, the woman, whose age is 35 appears ten years older. Her expression is fatigued, and she is literally worn out. The eyelids droop in flaccid folds. The hair is fine and very scanty, so scanty in fact that its poverty is unconcealed by the artifice of hair-dressing. There are brown pigmented patches on the skin. Sir Arbuthnot Lane would describe this woman as the victim of

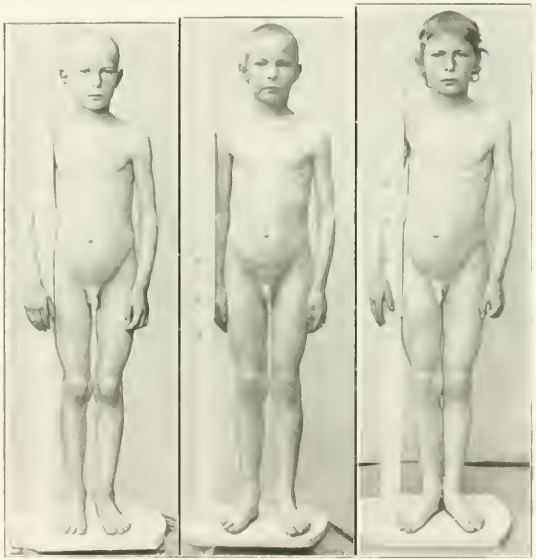


Fig. 12. *Benign thyroid insufficiency; infantilism of the Lorain type. Retarded growth, alopecia areata. Effect of thyroid extract upon the general processes of growth and upon the alopecia.*

Fig. 13. *Infantilism of the Lorain type; generalized alopecia. Result of thyroid medication continued for 9 months.*

Fig. 14.—*Mother of the* [illegible] *in* Figs. 12 *and* 13. *Chronic lymphatic thyroidism.*

Fig. 15.—*Mexican* [illegible] *insanity. Before and after a* [illegible] *course of treatment.*

chronic intestinal stasis, and he would be right, for she is habitually constipated. She suffers from frequent migraine, and she always feels cold. She complains of interscapular spinal neuralgia, especially in the morning. As we shall see later, she conforms to the type of slight chronic thyroid inadequacy. In the greater number of instances, children and adolescents who are the victims of nocturnal enuresis are thyroid inefficients. The woman under consideration wetted her bed until she was 16 years old. She now suffers from pollakisuria, and experiences an incessant need for micturition. She did not menstruate until the age of 18, a sign of marked backwardness in the development of the sexual organs.

In spite of my instructions, the boy, once his hair had grown, dropped the treatment, with the result that his hair again came out. It grew again, however, as soon as the thyroid treatment was resumed.

Many similar examples could be given, but enough has been said to show that thyroid stimulation is a necessary concomitant of growth; in other words, it is essential to the building-up of the cell.

CELL-DESTRUCTION.

After the cell has been in performance of its function for a certain length of time, it degenerates. The albumen-molecule breaks up into its component parts, and is eventually eliminated by way of the skin, the lungs, the intestine, and, more particularly, the kidneys, from which it is excreted in the form of water and urea. As long as the function of the thyroid is normal, this process of elimination continues. As soon, however, as thyroid activity is impaired, the products of decomposition cease to be carried off at the required rate, with the result that they accumulate *in situ* in the form of mucin, fat, and other bye-products. The cell becomes clogged with them, and a peculiar, hard œdema, which does not pit on pressure, is the result.

It is from this phenomenon that the term "myxœdema" is derived, a term used to include all maladies due to thyroid insufficiency. Where the condition is serious, this accumulation of waste products may attain enormous proportions. In other instances, it is barely appreciable, and the patient may

even be lean to emaciation. The accumulation is, however, none the less there. The process of infiltration may be intermittent, owing to the intermittent character of the thyroid exhaustion.

If thyroid extract is administered to a patient showing myxœdematous infiltration, the accumulation of waste products is immediately attacked, burnt up, and destroyed. The amount of the urea in the urine is enormously increased. The patient loses weight, and this loss is continued until the waste material is completely eliminated. After that stage has been reached, the weight remains stationary, even though the dosage be increased. If the treatment be suspended, combustion is retarded, and the weight rises until the earlier figure is again reached. Instances of the way in which the waste products of cell-decomposition may accumulate are, unfortunately, by no means rare. Let us take a case of well-defined thyroid insufficiency, such as that depicted in Fig. 15 (Plate VIII.).

This woman is 47 years of age. There is obvious infiltration of the face and of the entire body. She presents all the classical signs of myxœdema. When I first saw her, she weighed 10 stone 9½ lbs. At the end of 103 days of thyroid treatment her weight had fallen to 9 stone 9¼ lbs. She had thus lost 16 lbs. 11 ozs., 10¾ per cent. of her initial weight. The photograph shows very clearly the infiltration of the face, and the almost bestial expression which was imparted to it.

The woman shown in Fig. 16 is another instance of thyroid insufficiency. Her age is 63. Before treatment, she weighed 10 stone 13 lbs. 5 ozs. At the end of a course of treatment lasting 94 days, she had lost 21 lbs. 9 ozs., more than 12 per cent. of her initial weight.

Fig. 17 shows a woman who presents all the typical signs of acute myxœdema. She ascribes her condition to grief occasioned by the death of her husband 12 years ago. Her son has had several attacks of acute articular rheumatism. The infiltration is very considerable. At the end of 134 days, her initial weight of 12 stone 6 lbs. had fallen to 11 stone 8¾ lbs., a reduction of 11½ per cent.

The patient shown in Figs. 18 and 19 (Plate X.) is 51 years of age. He believes his condition to be the outcome of repeated attacks of acute articular rheumatism. He is suffering

Fig. 16.—*Thyroid insufficiency. Before and after a 94 days' course of treatment.*

Fig. 17.—*Thyroid insufficiency. Before and after a 134 days' course of treatment.*

Fig. 18.—*B. True myxœdema. Result of treatment with Cavell extract.*

Fig. 19.—*B. Cachexia. Before and after treatment.*

Fig. 2[illegible].—Thyroid insufficiency. *Effect of treatment upon the absorption of the infiltration.*

Fig. 2[illegible].—Thyroid insufficiency. *Age 49 years. Before and after a course of treatment extending over 270 days.*

FIG. 22.—Same as Fig. 21. *Profile.*

FIGS. [illegible]. *Pronounced thyroid insufficiency. Effect of thyroid extract on the nutrition.* Loss of weight, 15 per cent.

PLATE XIII.

Fig. 25.—*True myxœdema, age 63. Effect of treatment by thyroid extract. Reduction in weight, 20 per cent.*

Fig. 26.—*Severe myxœdema. Reduction in weight under thyroid medications 20 per cent.*

Fig. 27.—B. True myxœdema. Before and after treatment with thyroid. Initial weight 18 stone 0½ lbs.; reduced to 14 stone 2½ lbs.

Fig. 28.—B. Same as Fig. 27. Profile.

from myxœdema in a well-defined form. When he first came under treatment he weighed 15 stone 10 lbs. At the end of 98 days, he had lost 20¼ lbs., 12¾ per cent. of his initial weight.

The woman shown in Fig. 20 is 48 years of age. She has for some time been under treatment for a renal affection, probably Bright's disease. Her eldest brother has suffered from repeated attacks of acute articular rheumatism. Her initial weight was 10 stone 10 lbs. 10 ozs. At the end of 30 days she had lost 20 lbs., 13¼ per cent. of her initial weight. When treatment was inaugurated, this woman (Figs. 21 and 22) weighed 12 stone 7½ lbs. After 270 days, she had lost 24 lbs. 8 oz., 14½ per cent. of her initial weight. Notice how the profile has changed with the disappearance of the infiltration. The silly, almost ridiculous, expression has entirely disappeared, and the lines have become sane and normal.

The case shown in Figs. 23 and 24 illustrates a resorption which is even more marked. The patient's age is 52. In 203 days, the weight fell from 10 stone 11¾ lbs. to 8 stone 11 lbs. 13 ozs. Both the amount of the urine and the proportion of the urea excreted were very considerably increased. The disappearance of the facial œdema produced a change which was almost incredible. It seemed hardly possible that the face could belong to the same person.

The patient shown in Fig. 25 illustrates a very remarkable instance of true myxœdema. His age is 63. In 69 days, his weight fell from 15 stone 1 lb. 3 ozs. to 12 stone 1 lb. 3 ozs., an absolute loss of 3 stone, that is to say, 20 per cent. of his initial weight.

Fig. 26 illustrates a case of severe advanced myxœdema. The initial weight was 15 stone 11 lbs. At the end of a two-months' course of treatment with thyroid, he had lost 43 lbs. 13 ozs., 20 per cent. of his initial weight.

The two cases which follow show an even greater degree of infiltration.

B. (Figs. 27 and 28) is 63 years of age. He is very heavy, 18 stone 6½ lbs. He shows all the signs of typical myxœdema. The infiltration is enormous. Under treatment with thyroid, he lost 60½ lbs.—23⅝ per cent.—in 60 days.

Fig. 28 shows the patient in profile. The modelling of the bony structure, both facial and cranial, has reappeared with

almost sculptural clearness.

The patient who brings this series to a close weighed over 16½ stone. As the illustrations (Figs. 29 and 30) show, the infiltration of the face and neck, more especially of the nape, was enormous. Under the influence of thyroid extract his weight fell from 16 stone 8 lbs. 11 ozs. to 11 stone 6 lbs. 5 ozs., a total loss of 52 lbs. 13 ozs., 25¼ per cent. of his initial weight.

The cases which have been described illustrate very clearly the two main functions of the thyroid gland. These are the promotion of cell growth, and the elimination of the waste material which results from the destruction of the tissues. The thyroid gland watches over the maintenance of the organs through the medium of the trophic centres, and it controls the general chemistry of the entire organism. As a corollary to this activity, it may be said that the maintenance of temperature is dependent upon the integrity of the thyroid function. Hypothermia is an almost invariable accompaniment of even the slighter forms of thyroid insufficiency. Such patients, the younger ones more particularly, complain of chilliness of the hands and feet; they never feel warm, even in bed. In pronounced thyroid inadequacy, the morning axillary temperature may fall to 90° or lower, and the patient shivers in spite of the mountain of clothes and wraps with which he seeks to protect himself.

It is probable, however, that the thyroid gland performs functions which are of a nature even more delicate. Its secretion increases the resistance of the organism to infective diseases. It has been shown by positive experiment that in animals treated with an excess of thyroid substance the alexines are increased. As will appear later, a condition of thyroid inadequacy diminishes the plasticity of the blood, and induces a state of hæmophilia. This explains the profuse menstruation and the post-partum hæmorrhage, frequently of an alarming nature, which are observed in connection with subthyroidic women.

DISORDERS DUE TO THYROID INSUFFICIENCY.

Thyroid inadequacy in children is attended by a more or less complete arrest of the normal processes of growth,

Fig. 29.—*True myxœdema. Before and after* 61 *days of treatment with thyroid. The initial weight,* 10 *stone* 8 *lbs.* 13 *ozs., fell to* 11 *stone* 6 *lbs.* 5 *ozs.*

Fig. 30.—*Same as* Fig. 29. *Profile.*

Fig. 31. Myxœdema. Typical inadequate mistaken for Bright's disease. Before and after treatment with thyroid extract.

Fig. 32. Same as Fig. 31. Profile.

Fig. 33. Myxœdema, with predominant mental symptoms.

together with a varying degree of infiltration; the intensity of both symptoms depends upon the degree of the inadequacy.

In the adult, the lesion is confined to infiltration, the amount of which varies in accordance with the degree of thyroid insufficiency and the duration of the disease. With the few exceptions which I shall describe later, this infiltration has no tendency to spontaneous regression. Hence, those fortunate instances in which pregnancy is accompanied by resorption of the infiltrates are the more remarkable. The favourable phenomena in such cases are due to hypertrophy of the thyroid, by which pregnancy is accompanied.

Some women are never so well as when they are pregnant. Stimulation of the thyroid function does not, however, continue after the periods of gestation and lactation have passed. As soon as she has weaned her baby, the subthyroidic woman again falls into her former state of lassitude and torpor, accompanied by general infiltration. I have had to do with one such case, the history of which, from this point of view, was very remarkable. It is, briefly, as follows:—

Mme. B. (Figs. 31 and 32) was 42 years old when these photographs were taken. At the age of 28, as the result of chill, she had marked swelling of the hands and feet. She had had albumen in her urine, and had, in consequence, been treated for Bright's disease. In spite of the treatment, however, she had made no progress, and for years she dragged herself about, weary, somnolent, worn, and aching in every limb. She became pregnant, and her symptoms were immediately relieved, the amelioration lasting during the entire period of pregnancy and lactation. She suckled her child for two years. After weaning, her former state gradually reasserted itself; she became apathetic and depressed, while the rheumatoid pains returned with more than their former intensity.

It will be seen from the portrait that the hair is very scanty. The features are puffy; the amber complexion is reminiscent of Bright's disease; there is constipation and headache; the teeth are bad; in the evening, there are shivering fits which have been ascribed to fever. All these symptoms improved under treatment with thyroid extract.

In certain cases of slight inadequacy, spontaneous ameliora-

tion after the menopause has been observed. The migraine, which has proved the scourge of a lifetime, may abruptly disappear at the age of 50. The reason for this will appear later, when the influence exercised by the thyroid gland upon the sexual life of women comes under consideration. Menstruation, or rather the inhibition of menstruation, appropriates a large proportion of thyroid secretion. During the menstrual period, and during that period only, many women present symptoms of subthyroidism, headache, migrane, constipation, etc., together with a certain hoarseness denoting slight infiltration of the vocal cords. The menopause restores to the general economy a large amount of thyroid secretion which, under other conditions, would be employed in maintaining the plasticity of the blood.

THE MUSCULAR TISSUE.

Let us now turn our attention to the process of infiltration, as it affects the organic tissues.

By reason of its burden of fat and mucin, the volume of the muscular cell becomes increased. The contractions are retarded, and muscular drainage becomes sluggish. Contraction causes pain, and there is consequent stiffness and fear of movement. The connective tissue surrounding the contractile cellule, which forms the termination of the muscle itself and ensures its continuity with the tendons, aponeuroses, and articular ligaments, also undergoes infiltration, and the difficulty of movement is still further increased. This applies equally to the voluntary and involuntary muscles.

The muscular *malaise*, which results from the process of infiltration, is expressed subjectively by pain of a "rheumatoid" character. This must not be confused with so-called "rheumatic" pain, which is referable to causes outside the scope of this article. Accounts are sometimes met with, notably in the works of French authors, of the results obtained by the exhibition of thyroid extract in the management of articular rheumatism, both chronic and acute. These should, however, be accepted with reservation. Thyroid extract does not relieve pain in the muscles, ligaments, and joints, unless that pain is due to thyroid perversion; in other words, to specific myxœdematous infiltration. It must be

borne in mind that thyroid extract is essentially specific in its action, and that it can only take effect when there is thyroid inadequacy or thyroid suppression. Rheumatoid pain constitutes one of the most constant symptoms of thyroid insufficiency, whether malignant or benign.

Thirty years ago, when I was a young man embarking on my career, and entirely oblivious of any condition partaking of the nature of thyroid inadequacy, I had as a patient a woman whose chief symptom consisted in violent rheumatoid pain unaccompanied by fever. All the muscles were stiff and painful, the joints were swollen, and the gait was heavy, suggesting ankylosis. The pain in the back was particularly aggressive. I worked at that patient for a long time, subjecting her, with all the ardour of the neophyte, to every conceivable form of treatment. At last she resigned herself to her fate, and sent for me only when the pain was unendurable, and the swelling of the wrists and knees became alarming. Eventually she changed her place of abode, and I lost sight of her.

Now, she had a very peculiar intonation of voice, identical with that of the myxœdematous patients who, later, came to form my great preoccupation. I managed to trace her, and discovered that, not only her voice but many other traits, pointed infallibly to the presence of myxœdema. Thyroid treatment was immediately inaugurated. I had not expected that the generalized pain and stiffness would disappear, for I did not at that time associate these symptoms with thyroid inadequacy. Nevertheless, they did disappear, slowly and progressively, and with them went a very distressing oppression from which she had always suffered, and which I had ascribed partly to obesity and partly to pulmonary emphysema. All the symptoms having disappeared, I regarded her as cured, and suspended the treatment. Gradually, however, the pain and sense of oppression returned, and treatment was resumed, with the result that the symptoms were again effaced.

These rheumatoid pains, from which the patient had suffered since she was a young woman bearing children, were from beginning to end nothing but a simple manifestation of thyroid inadequacy. They were the direct outcome of muscular,

ligamentary, and articular infiltration. Fig. 33 shows the patient as she appeared immediately before I instituted the thyroid treatment. There was uniform infiltration of the face, the lips were thickened, and the hair and eyebrows very scanty.

Muscular infiltration, which occurs in an extreme form in true myxœdema, is present, though in a minor degree, in the slighter forms of thyroid inadequacy. In such patients, the pain is generally localized in the back. It is characteristic and pathognomonic of this rachialgia that, owing to the chilliness resulting from nocturnal inanition and activity, the pain is more intense at night. It usually settles between the shoulder-blades, though pain in the sacral and dorso-lumbar regions is not infrequent. In the latter instances, the pain is usually ascribed to utero-ovarian sources.

There are some women who, morning after morning, rise early in the hope that escape from bed will mean escape from pain, and who drag themselves about in as broken a condition as if they had spent the night strapped to a board. Movement and food induce a certain relief in the course of the day, and in the evening, after a good dinner, the pain completely disappears. These patients like wine with their dinner ; they instinctively seek the sense of well-being which it bestows.

Pain in the shoulders and arms is not infrequent, and the patient complains of the difficulty of doing her hair. Or the knees may be affected, patients being unable to rise from a kneeling or sitting position. Pain in the sole of one or both feet is common, and this is significant in connection with what has been said concerning flat-foot and the relaxation of the articular ligaments.

THE NERVOUS TISSUE.

In myxœdematous infiltration, whatever its degree, the nerve-cell is never destroyed in the same way as in hæmorrhagic foci, and in necrosed patches due to embolism. It merely suffers derangement of nutrition, and of the processes by which waste material is eliminated. It becomes infiltrated, and it also undergoes compression, as the result of the infiltration of the connective tissue surrounding it. Hence,

the transmission of motor and sensory impulses, both voluntary and involuntary, though delayed, is in no sense abolished. The reflexes are tardy, but they are present.

The condition of the nerves is expressed subjectively by neuralgias and by lightning pains of a neuritic type. The patients are able to distinguish between the two classes of pain. Cardiac pains, painful irradiations in the brachial plexuses, anginiform pains, and pseudo-angina pectoris are also complained of.

Owing to the relative incompressibility of its elements, the nervous system is affected at a very early stage of infiltration, however slight the process may be.

True myxœdema presents a veritable chaos of symptoms; giddiness, a dazed sensation, noises in the ears, headache, migraine, loss of memory, mental confusion, melancholia, loss of consciousness, loss of equilibrium. The sudden falling down, the somnolence, and the fits of coma lend a certain resemblance to the serous apoplexy of Bright's disease, with which the condition has sometimes been confounded. The resemblance is the more striking from the fact that, in true myxœdema, albumen is frequently present in the urine.

In benign myxœdema, the array of symptoms is by no means so formidable. Of these the most striking are the morning headache, the migraine, the giddiness, the noises in the ears, and the somnolence.

The headache of thyroid insufficiency assumes two forms. Sometimes it originates in the frontal sinuses and extends over the orbits, always, however, remaining frontal. In character, it resembles the early headache of coryza. Sometimes, the pain originates at the occiput, and a painful centre in the neighbourhood of the occipital nerve lends to it the character of a neuralgia. From the occiput, it invades the corresponding portion of the brain, and the patient describes the attack as one of migraine. The pain differs from true migraine, however, in this, that it is more intense in the morning, and disappears entirely in the evening after a good dinner.

Patients become so accustomed to this form of headache that they frequently omit to mention it unless asked. They usually ascribe the falling of their hair to incessant headache,

and in this they sometimes receive the support of the doctor, who describes the malady as "epicranial rheumatism." The least fatigue, the slightest degree of perspiration, or the faintest draught are sufficient to provoke an attack of occipital headache. Trigeminal neuralgia, provoked by the wretched condition of the teeth, is frequent; and headache above and below the orbits is a common feature of slight hypothyroidism.

Giddiness is one of the most constant and distressing features of thyroid insufficiency. When the condition is very marked, it is the frequent cause of falls, from which fractures and dislocations are liable to result. In the slighter forms, the symptom makes its appearance at a very early stage.

In connection with the noises and buzzing in the ears, which have been included among the early symptoms of thyroid inadequacy, it is interesting to note that, in 1898, George Murray pointed out [1] that certain hallucinations of sight and hearing are not uncommon in a condition, which he describes as "early thyroid fibrosis." The patients see objects of ill-defined outline resembling cats, rats, or mice, which run rapidly across the floor while, at the same time, bright points of light appear in the field of vision. They also hear voices and the ringing of bells. According to Murray, patients show a disinclination to discuss these symptoms. Is this due to the fact that the hallucinations strongly resemble those associated with alcoholism?

Since my attention was directed to this point, I have questioned several patients, and have succeeded in confirming Murray's statements. Noises in the ears are a frequent accompaniment of thyroid insufficiency, and they disappear under treatment. I believe that the source of this trouble is largely to be sought in infiltration of the nervous centres. At the same time, infiltration of the aural mucosa, the Eustachian tubes, and the naso-pharynx are probably important contributory causes.

Somnolence is an interesting feature of thyroid inadequacy. Subthyroidic children, including those of the Lorain type, sleep very heavily, and are not easily disturbed. It is among these that the subjects of nocturnal enuresis are found. In adults, the degree of the somnolence is really incredible. They

[1] *British Medical Journal*, October 10, 1898, p. 944.

sleep in any place and at any time, and have even been known to drop off in hospital waiting-rooms; yet they never feel rested and refreshed. In the morning, they wake with a heavy head and pain in the nape of the neck. It is probable that, under physiological conditions, the thyroid gland neutralizes, at least in part, the toxins which result from organic activity. The sleep which follows a day of hard and healthy work is probably the outcome of the resultant inanition. During the night, the thyroid recovers its powers and, when morning comes, it is rested and refreshed. In the myxœdematous subject, however, this restoration is incomplete, and he feels more fatigued in the morning than he does at night.

There are several points of interest in connection with the mental troubles brought about by infiltration of the nervous centres. In the case of children suffering from true myxœdema, the poverty of ideas, which may amount to idiocy, is explained by inhibition in the growth and development of the nervous centres. In slighter cases, there is an extreme turbulence, with a disposition to throw down and break everything. Infantile subjects of the Lorain type are rather more intelligent, but they succeed in retaining very little, and remain puerile in their tastes and conversation for a long time after reaching the adult state. In spite of a certain vivacity of spirit, which is not uncommon amongst them, these people have no depth, and their thyroid inadequacy is readily divined. Their handwriting is absolutely childish, a characteristic which frequently persists through life.

In adults, the infiltration of the nervous centres determines a slowness of ideation, a partial or entire loss of memory, and a difficulty in expression. The patient knows what he wishes to say but the cerebral image is clouded. The trouble is aggravated by the difficulty of articulation, due to thickening of the tongue and buccal mucosa.

On the psychic side, melancholy is the predominating note of the myxœdematous subject. He is the victim of a resigned and silent sorrow. His reason, on the other hand, is never clouded, and his better self preserves its full perceptive powers; but the expression of his opinion is so fatiguing to him, that he ceases to attempt it. These people are frequently reproached for their general negligence and their inattention

to the duties of their occupation. This is unjust, for, as a matter of fact, the obligations of daily life are more than they are fitted to perform.

In slight thyroid insufficiency, the psychic condition is expressed by an extremely disagreeable tendency to profound pessimism. Women of this type get into a state of panic about nothing, see everything through black glasses, and live on the edge of a species of chronic despair. Among the richer classes, for whom social obligations are of a somewhat superficial character, this is, after all, a trifling matter. It is among these that the uncured and incurable invalids are found. Misunderstood by everyone, the sympathy of their intimates alienated by incessant complaining, they live on in a state of complete indifference to their surroundings.

In the case of the lower classes, it is not difficult to guess at the condition of the household, when the mother is a thyroid insufficient. The disorder, the lack of economy and of organization, the dirt and the waste combine to create a veritable inferno. For several days out of the week, the woman is nailed to her bed by migraine, while her little energy is drained away by frequent and profuse menorrhagia. There are many families, which are free from the taint of alcoholism or vice, but which are yet unable to succeed in making both ends meet. In the vast majority of such cases, the key to the situation lies with the subthyroidic diathesis.

THE BONY TISSUE.

In spite of its apparent immobility, the bony tissue does not escape the effects of thyroid insufficiency. All surgeons know that, in certain individuals, fractures heal badly or not at all, and it is customary to combat this troublesome complication by the empirical exhibition of thyroid extract. If these patients are carefully examined, they will be found to show symptoms of general thyroid inadequacy, and this is invariably the case with those who derive benefit from thyroid medication.

A rachitic curve in the tibias is almost invariable in subthyroidic children. That this symptom disappears under suitable thyroid treatment, is amply shown by the histories cited in the earlier portion of this article. Conclusive proof of

PLATE XVII.

Fig. 34.—Skiagram of the hand (palmar aspect) of an infantile subject of the Louvain type. Age 24, height 4 ft. 7 in. The epiphyses, which are still transparent, are indicated by means of arrows. Prognosis: possibility of growth.

Plate XVIII.

Fig. 35. *Infantile subject of the Lorain type. Age 24; height 4 ft. 7 in. Effect of thyroid treatment upon the growth.*

PLATE XIX.

Fig. 36. *Persistence of the epiphyses. Possibility of growth*

PLATE XX.

Fig. 55.—*Chondro-osteoma of the epiphysial cartilage. Junction of growth believed to be impossible.*

the effect produced by thyroid inadequacy upon the processes of ossification, is afforded by the persistence of the epiphyses in myxœdematous dwarfs, at an age when they are no longer perceptible by means of skiagrams in persons of normal growth.

The X-rays supply an invaluable method of determining the possibility of growth, under thyroid treatment, in children of retarded or arrested development. Doctors are occasionally consulted on this point by parents, who have become alarmed because their child has stopped growing. Some time ago, I pointed out the diagnostic value of the X-rays in this connection.[1] The method is absolutely reliable, and excludes the possibility of error.

The young man shown in Fig. 35 is 24 years of age. He is exceedingly small, his height being only 4 ft. 7 in. He is so weak that he can scarcely walk, and the emaciation is extreme. He is an infantile subject of the Lorain type. His gait is stiff, and he moves all in one piece, like a wooden figure. His growth ceased at the age of 14. The skiagram (Fig. 34, Plate XVII.) shows that the epiphyses have not undergone ossification and that growth is therefore possible. Under treatment with thyroid, the boy did, in fact, begin to grow. In six years, he grew 6 inches. The sexual organs attained complete development within a period of six months.

Fig. 36 shows the hand and wrist of a boy of 19, whose height was 4 ft. 1⅛ in. The genitals were almost infantile. He was somnolent, mentally dull, and suffered from severe migraine and neuralgia. The epiphysial cartilages were perfectly transparent, pointing to a possibility of renewal of growth. The prognosis was confirmed by the results of treatment with thyroid extract. At the end of one year, he had grown 2⅝ in.; at the end of two years and nine months, 4¾ in., his height being 5 ft. 2½ in.

Fig. 37 shows the hand of a boy of 18, whose height was 4 ft. 11 in. The skiagram shows very clearly the complete ossification of the epiphyses, pointing to the impossibility of a renewal of growth. The prognosis was confirmed by the

[1] "Diagnostic de la possibilité d'une reprise de croissance dans les arrêts et retards notable de la croissance," avec planches. *Bulletin de l'Académie Royale de Médecine de Belgique*, 1896, Vol X., 4th Series, No. 8, p. 564.

results of treatment.

The young girl, the skeleton of whose hand is shown in Fig. 38, is 18. Her height is 4 ft. 10½ in.; she ceased growing when she was 14. The epiphyses are ossified, and treatment has been negative.

THE CARTILAGINOUS TISSUE.

The cartilaginous tissue undergoes well marked specific infiltration. The joints of a myxœdematous subject are persistently stiff and painful. If the hand is applied to such a joint when flexed, there will be a sensation like the crackling of frosted snow. This is a very characteristic sign; indeed, it is almost pathognomonic, and it is most readily detected in the knee-joint. Occasionally the patient is himself aware of a crackling sensation in the cervical vertebræ. This phenomenon was first described by Professor Verriest of Louvain.[1]

The painful sensations in the joints are very difficult to disperse, and they are the last symptoms to disappear. A patient of mine, an ecclesiastic, was the victim of myxœdema in a very pronounced form. For some months after a complete cure had been established he continued to complain of stiffness in his knees, the ritual genuflexion being still very difficult for him. Gradually, however, the stiffness passed away (Fig. 26, Plate XIII.). This postponement of the restoration of function is probably explained by the tardiness of the exchanges in the cartilaginous tissues.

THE GLANDULAR TISSUES.

The glandular tissues, which play so important a part in the general economy, are also subject to the infiltration of their elements and of the connective tissue surrounding them. In thyroid inadequacy, the secretion of the sweat-glands is entirely abolished, and the liver becomes appreciably congested.[2] The biliary cells do not adequately perform their function, and, consequently, the bile ducts become choked.

[1] *Bulletin de l'Académie Royale de Médecine de Belgique*, 3rd Series, Vol. XX., No. 5, p. 330.

[2] The excellent writings of M. A. Ver Ecke, of the Gand University, upon lesions of the liver and kidneys in subthyroidic animals (*Bull. de l'Acad. Royale de Belgique*, October 1897, pp. 666, 668, 698, 704) are very interesting in this connection.

PLATE XXI.

Fig. 38. Complete ossification in a girl of 18. Removal of growth is impossible.

Fig. 30.—*True myxœdema, three days before death.*

Fig. 40. *Distended gall bladder of the woman shown in* Fig. 39. *The excretory duct is blocked by a large calculus. The distal extremity of the bladder was on the point of gangrene.*

Fig. 41.

Fig. 42.

Figs. 41 *and* 42.—*True myxœdema, before and after treatment.*

The bile passes into the blood, giving rise to the icterus of myxœdematous subjects (amber coloration of the skin). Biliary calculi are frequent. For my own part, I attach great importance to hepatic disorders in thyroid insufficiency.

Some light is shed upon this point by the following histories of cases.

Fig. 39 shows a woman suffering from true myxœdema. The disease was in its last stage, and she died three days after she came under my care. I was unable to administer thyroid extract. A post-mortem examination was made. The gall-bladder was on the point of rupture, being distended and very attenuated at the superior pole ; it contained a large calculus which, while permitting the entrance of bile, effectually prevented its exit. (Fig. 40.)

I was very much struck by this finding, and since then I have carefully tested the sensibility of the liver, and especially that of the gall-bladder, in all myxœdematous subjects. Very frequently, indeed almost invariably, tenderness is discoverable ; this disappears under treatment.

A calcareous gall-bladder is no unfamiliar spectacle in the post-mortem room. I have, however, reproduced the one I found on that occasion, in order to emphasize the significance of hepatic disorders in myxœdema, whether true or of the *forme fruste*. The possibility of congestion of the liver and of the presence of stone or sand in the gall-bladder should never be lost sight of. The amber complexion peculiar to myxœdematous subjects is, in reality, an attenuated jaundice arising from the biliary conditions.

Figs. 41 and 42 illustrate a case of well-defined true myxœdema. The patient is 40 years of age. Her father died of rheumatism with albuminuria. She is the mother of six children. The eldest girl is subject to metrorrhagia. Two sons suffer from acute rheumatism in a very severe form. She has no appetite. "I should never eat," she says, "if I followed my inclination." She has menstrual floodings, headaches, and frequent shivering fits. The temperature in the mouth is a fraction over 96°.

The puffiness is extreme ; the hair is well-preserved ; the teeth are good and attractive. There is melancholy, apathy, difficulty in pursuing a train of thought, in speaking, and in

moving. She became an in-patient and, at the end of a six weeks' course of treatment, was discharged cured. Her appearance had altered to such a degree that she was not recognizable as the same woman. Since that time, she has continued the treatment intermittently. When she neglects it for long, the return of the malady is announced by a sensation of heaviness in the epigastric region, difficulty in stooping, tenderness in the neighbourhood of the liver, and disinclination for food. Upon one occasion, after prolonged neglect of the treatment, I was fetched out to her in the night. I found her suffering from violent biliary colic. Oil and morphine at the time, with subsequent resumption of the thyroid treatment, put her right again.

The scantiness of the intestinal secretions combines with the muscular paresis of the visceral organs to produce constipation of the most obstinate kind. Excessive fermentation and flatulence result, with the usual accompaniments of tympanitis, gastric distension, eructation, rumbling, etc.

THE EPIDERMIC AND EPITHELIAL TISSUES.

Considerable interest is attaching to the changes which take place in the epidermis and epithelium. The epidermis, being insufficiently nourished, desquamates and scales off. There is premature baldness. In benign myxœdema, the hair is fine and brittle, and tends to premature greyness. The beard is scanty, fine, and lamentably ill-nourished. The striking changes in the hirsute appendages, which are common in myxœdema, are of considerable diagnostic value, revealing as they do the nature of the malady at a first glance.

Fig. 43 shows a myxœdematous subject whose age is 42. The hair is very sparse indeed. The face is infiltrated, and the eyelids are raised only by an effort. The eyebrows have disappeared. The lips are thickened. On the forehead is a brown pigmented band, and there are patches of pigmentation on the neck and face. The infiltrated muscles and ligaments of the neck are unable to support the weight of the head, which falls forward. To raise it, the patient is compelled to bend his body backwards. He complains of rheumatoid pains and perpetual chilliness, in spite of the fact that he is loaded with warm clothing both by day and night. The breath is

Fig. 43.—*True myxœdema. Baldness arising from thyroid insufficiency. Pigmentation of the skin.*

Fig. 44.—*Same as* Fig. 43. *Full face. Before and after treatment.*

Fig. 45.—*Myxœdema*, forme fruste. *Baldness over the temples*

Fig. 45. Same as Fig. 43. Occipital baldness. Effects of treatment.

Fig. 47.—Slight thyroid insufficiency. Eyebrow sign.

Fig. 48. Exophthalmic edema with marked affection of the hair and eyebrows. Before treatment.

Fig. 49. Same as Fig. 48. Profile.

œtid, the teeth bad, and the gums red and inflamed. He speaks with difficulty, and replies to questions only after a long pause. He opens his mouth very widely, revealing the movements of his tongue, but no sound issues. It is not until after a prolonged display of buccal gymnastics that he succeeds in slowly bringing out his words. His weight is 10 stone 11 lbs. 13 ozs.

Under thyroid treatment this patient lost 22 lbs., and all the symptoms became very much ameliorated. The daily loss in weight was 16½ oz. to 2 lbs. The hair grew rapidly, and muscular contractility was re-established. The mental attitude became more hopeful, especially after he found that he could again lift his head. He was overjoyed at the prospect of recovery, which was complete in about two months.

In all subthyroidic subjects, the nails are striated and brittle. In true myxœdema, they are split and broken. The teeth are almost invariably in a lamentable condition, carious, with receding gums, and coated with a greenish tartar which looks like fat. The gums are red and inflamed; at the level of the dental interstices, they are continued in polypiform prolongations.

The eyebrows, especially in the outer third, are very sparse, which lends to the face an expression of extreme foolishness, and gives it an imbecile character. In benign insufficiency, the hair may fall prematurely, but in the majority of instances it whitens. There is the same dental imperfection and chronic deterioration of the gums as in true myxœdema, but in a minor degree.

In all myxœdematous conditions, whether malignant or benign, the falling of the hair follows a method and sequence which may be regarded as specific. The hair disappears at first from above the forehead; later, it recedes from the nape of the neck. This is very well shown in Figs. 45 and 46.

The scantiness of the eyebrows is a constant sign. In myxœdema *fruste*, it appears at a very early stage, and is described as the "eyebrow sign." It lends to the face an expression of perpetual astonishment, and, unlike baldness, the sign is one which it is impossible to conceal.

Fig. 47 shows a young woman of 24. Since her last confinement, four months ago, she has incessantly lost blood. She has been curetted several times. I should not have

associated her condition with thyroid inadequacy, had I not been struck at the first glance by the absence of her eyebrows. The frontal baldness is hidden by the arrangement of her hair. She suffers a good deal from migraine and occipital headache; she always feels cold; she is much troubled with flatulence; menstruation has always been very profuse. I exhibited thyroid extract, and, at the end of a fortnight, the discharge had ceased.

Figs. 48 and 49 (Plate XXIV.) illustrate a very interesting case of true myxœdema, with marked affection of the hair. In addition to scantiness on the frontal and occipital borders, the hair had become very thin along the sagittal line. The baldness was partly disguised by a blackish incrustation, which had invaded the whole of the upper portion of the scalp. The eyebrows were very sparse. Treatment with thyroid extract produced astounding results.

This woman comes under the heading of advanced myxœdema. She was always tired, constipated, and somnolent. Her rheumatoid pains never left her. The slightest movement sufficed to make her breathless. The face was infiltrated, the eyelids heavy, the lips hideous. Under treatment with thyroid, she lost 22 lbs. very rapidly, and to-day, after four months, she is a changed being, both physically and mentally. She has gained in courage, purpose, and gaiety. She has even become a little vain, and cannot believe that she was ever as ugly as her portrait shows.

Figs. 50 and 51 supply an excellent example of the eyebrow sign, and of the effect of thyroid insufficiency upon the condition of the hair. This woman is only 39, but she appears to be much older. The face is infiltrated, the skin of an amber-yellow with red patches on the cheek-bones. The trophic derangement is chiefly perceptible in the condition of the hair and teeth. The occipital portion of the scalp is almost entirely denuded. There is a persistent sensation of chilliness and chronic constipation. There are generalized pains attributed to rheumatism. The speech is drawling, and the voice is of the characteristic timbre. Weight, 11 stone 4 lbs. Under treatment she lost 22 lbs.

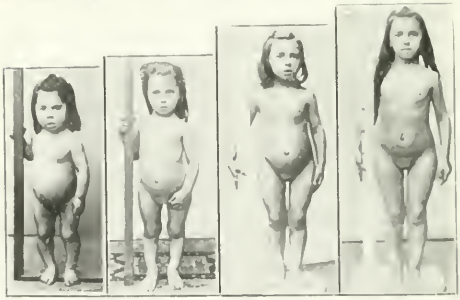
This patient has prematurely lost her eye-lashes. The

Fig. 50.—*Myxœdema with marked affection of the hair.*

Fig. 51.—*True myxœdema. Cas wary neck.*

Fig. 52.—*True myxœdema. Influence of thyroid extract.*

Fig. 53.—Daughter. Fig. 52.—*Benign myxœdema, before and after treatment.*



a. *b.* *c.* *d.*

Fig. 54.—*W. True infantile myxœdema. Arrest of growth. Effects of thyroid medication.*

Fig. 55.—*True infantile myxœdema. After 14 years of treatment.*

Fig. 56.—*Benign myxœdema. Married lady.* (Figs. 54 and 55).

desquamated palpebral margins are insufficiently protected from the erosive action of the lachrymal secretion. There is blepharitis of subthyroidic origin.

The unsightly blepharitis of old people is sometimes due to a similar cause. In one instance, where all other means had failed, I obtained a radical cure in a very few days by the local application of adrenalin and the exhibition of thyroid extract.

The skin of the patient shown in Figs. 50 and 51 (Plate XXV.) is generally thickened, infiltrated, and chilly. She is subject to various eczematous affections.

The form of infantile eczema, commonly known as "milk-crust," which is the despair of mothers and doctors, yields very readily to a treatment of thyroid extract with arsenic, when the subject is of subthyroidic habit. This also applies to psoriasis and to certain forms of eczema.

The mucous membranes of the subthyroidic subject—whether buccal, labial, lingual, nasal, pharyngeal, laryngeal, aural, or œsophageal—undergo infiltration. It is easy to appreciate the disorders engendered by such a state of things in the processes which control enunciation, deglutition, and hearing. The swelling of the mucosa of the isthmus of the fauces and of the œsophagus is sometimes so marked as to interfere with the act of swallowing.

It is well to remember that infiltration of the tonsils sometimes gives rise to considerable hypertrophy of these organs. Chronic painful tonsillitis is frequent in subthyroidic subjects, and there are few of the victims of infantilism who are not affected by adenoid growths.[1] The lymphoid tissue of Waldeger is peculiarly adapted to myxœdematous infiltration. We shall return to this point later.

In very severe cases of advanced myxœdema, when death is imminent, the tongue, which is enormously swollen, falls back into the throat. Air is thus prevented from entering the trachea, although the thorax continues to make respiratory movements. This ineffectual pumping exactly resembles that sometimes seen in chloroform narcosis. After five or six

[1] Hertoghe: "Vegétations adénoïdes et Myxœdème," *Bull. de l'Acad. Royale de Belg.*, meeting on March 26, 1906.

false inspirations, there is a spasm of the tongue and pharynx, and air once more passes the glottis. Normal respiration is re-established for a certain time, until the pharynx is again blocked by the tongue, when the phenomena are repeated. An uninformed observer might easily mistake this respiration for that of the Cheyne-Stokes type.

The epithelium participates in the general deterioration. It falls prematurely, thus exposing the walls of the cavities (gall-bladder, urinary bladder) to the irritant effects of the fluids which they contain. The gall-bladder becomes tender or painful, and the accumulations of desquamated epithelium form centres for the accretion of calcareous deposits. Cholelithiasis is a frequent accompaniment of true myxœdema. It also occurs in slight myxœdema, though in a less severe form.

Owing to the incessant denudation of its squamous covering, the bladder is more sensitive than under normal conditions to the irritant action of the urine. To this is largely due the nocturnal incontinence of children, and examination reveals the presence of an enormous quantity of squamous cells in their urine. These children are invariably subthyroidic, and the stigmata of a more or less clearly defined thyroid inadequacy are generally to be observed in the parents, more particularly in the mother. As the child grows up and its thyroid resources develop, the infirmity is gradually overcome. A residuary legacy in the form of pollakisuria (the need for frequent micturition) is almost invariable in the case of girls.

To return for a moment to the characteristic subnormal temperature of thyroid insufficiency, this may result from diminution or retardation in the combustion of mucin and fat. Or it may be due to infiltration of the nervous centres which control the regularization of temperature. It is certain that, in true myxœdema, if large doses of thyroid extract are exhibited at the beginning of treatment, when the economy is loaded with an enormous mass of infiltrated material, a notable rise in temperature, which may even be mistaken for a feverish attack, will take place. This is probably the direct result of the ultra-rapid combustion of the infiltrated material.

The subject of thyroid insufficiency is extremely conscious

of his subnormal temperature. This undergoes a diurnal depression, and its effects are most keenly felt at about 4 or 5 o'clock in the afternoon. The patient is attacked by violent shivering fits, with a sensation as if cold water had been poured down his spine. The phenomena are usually wrongly interpreted, and the patient is dosed with quinine—obviously a useless measure.

Hypothermia is present, though to a less marked degree, in the slighter forms of myxœdema It takes the form of general chilliness, and, in women and children more especially, the hands and feet are always cold. A common sign is insensibility, impotence, and pallor of one or more fingers—"dead" fingers as they are called.

THE CARDIO-RESPIRATORY SYSTEM.

The results of infiltration upon organs of a more complex nature are well seen in the case of the cardio-respiratory system.

Paresis of the heart-muscles, paresis of the inspiratory and expiratory muscles of the thorax and diaphragm, painful infiltration of the nervous ganglia at the base of the heart, derangement of the cardiac innervation, infiltration of the substance of the lungs and of the mucosa of the bronchi and bronchioles, —such are the conditions which obtain in myxœdema. The consequences are briefly as follows.

The dyspnœa of true myxœdema in some instances surpasses description. Even with a rest half-way, the patient can scarcely climb a short flight of stairs, and staggers into my consulting-room speechless for want of breath. Clinging to any piece of furniture within reach, he indicates by signs that, until he has rested, he is incapable of uttering a word.

In slight thyroid insufficiency, the oppression is less extreme. It may be intermittent, showing itself only under exceptional fatigue, a degree of fatigue which corresponds to an exaggerated demand for thyroid secretion on the part of the impoverished organism. Such intermittent dyspnœa is frequently mistaken for asthma. There is no doubt that many asthmatics are the subjects of thyroid insufficiency. Unexpected cures in asthma, as the result of thyroid medication, have been described by

several authors. While admitting that the patients showed all the signs of subthyroidism, these authors, nevertheless, persist in describing the condition as "neuro-arthritic asthma," which, to say the least, is hardly logical.

A word as to the supposed dangers of thyroid medication. The organ chiefly affected by the toxic effects of thyroid extract is the heart. The danger of cardiac over-stimulation by a careful thyroid therapy is, however, negligible. Many sufferers from Graves's disease are able to resist, over a long period of years, the results of a very intense tachycardia. In the course of my observations of thyroid inadequacy, the conviction has gradually been forced upon me, that the physiological stimulant of the heart is supplied by the thyroid secretion. It is, in a certain sense, the necessary tonic, the normal digitalis, by which cardiac activity is promoted and maintained. Where other signs of thyroid inadequacy are present, I do not hesitate to exhibit thyroid extract in cases of weak contractility and tendency to syncope, and I may say that the treatment has never failed me.

There are cases of true myxœdema, in which the predominating symptom is cardiac pain. Such a case is illustrated by a patient of mine. During the earlier part of the treatment, the cardiac pain became much intensified, owing undoubtedly to the rapid disappearance of the infiltration from the cardiac muscles and nerve-centres. On no account should the physician permit himself to become alarmed and to discontinue the treatment. In the case referred to, the original symptoms disappeared in the course of a few days.

THE GASTRO-INTESTINAL SYSTEM.

The entire gastro-intestinal system reacts very strongly to the infiltration of its elements, whether muscular, nervous, secretory, or mucous. Infiltration of the muscular tissues nduces peristaltic paresis, leading to retention of waste materials with consequent fermentation and constipation. In delicate subjects with weak abdominal walls, constipation results in ptosis of the viscera, notably of those organs which are most heavily loaded, namely, the stomach and large intestine. The dropping of the intestine stretches the mesenteric bands

by which it is normally supported. The precise spots at which these hypertrophied bands are attached to the viscera have been determined by Sir Arbuthnot Lane. Immediately on either side of them the intestine falls away, and in this manner kinks are formed. The most important of these kinks are the ileo-cæcal, the jejuno-duodenal, and the pyloro-duodenal, the presence of which has been incontrovertibly demonstrated by Lane. Morbid exaggeration of the hepatic and splenic curves of the colon, and abnormal curvature of the pelvic colon, have also been observed.

Imperfect intestinal drainage gives rise to intestinal toxæmia, which reacts upon the already enfeebled thyroid gland and intensifies the prevailing conditions of inadequacy. As a matter of fact, many of the symptoms attributed by Lane[1] to chronic intestinal stasis are identical with those which, since 1899,[2] I have included in the symptom-complex of benign chronic subthyroidism. These are hypothermia, uncontrollable headache, rheumatoid pain and neuralgia, mental depression, dyspnœa, asthmatic attacks, premature greyness and baldness, dental caries, choleolithiasis, and brownish pigmentation of the skin.

In severe thyroid inadequacy, there is absolute want of appetite, and the aversion for food is unconquerable. Meat is especially distasteful. In common with the rest, the secretory flow from the intestinal glands is diminished, and this tends still further to aggravate the constipation. It is by no means rare to find subthyroidic individuals who go for 5, 10, even 25 days without having their bowels open. Infiltration of the intestinal mucosa tends to reduce the calibre of the bowel, while disorders of the biliary apparatus still further aggravate the general gastro-intestinal derangement.

In a recent publication,[3] I pointed out that there is a

[1] La Stase intestinal chronique, par Sir Arbuthnot Lane. *26th Surgical Congress, Paris*, 1913. *Lectures, Memoranda and Discussions*, p. 595, Paris. Alcan.

[2] De l'hypothyroïdie bénigne chronique du myxœdème fruste. *Bull. Acad. Méd. de Belg.*, March, 1899, Vol. XIII., p. 231; etiam in *Nouvelle Iconographie de la Salpêtrière*, 12th year, No. 3, 1899; with 29 photographs and 7 pictures.

[3] Appendicite et Hypothyroïdie. *Bull. Acad. Méd. de Belg.*, meeting of January 31st, 1914.

noticeable tendency to appendicitis among the subjects of thyroid insufficiency. Demonstrable thyroid inadequacy is sufficient, in many instances, to account for chronic appendicular conditions of a more or less dangerous character.

To what must this undoubted tendency to appendicitis be ascribed? Is it the result of chronic constipation, of the habitual overloading and consequent ptosis of the cæcum? Ptosis is attended by the formations of adhesions, by the creation and multiplication of which nature seeks to guard against a yet more radical descent. It is well known that, not only are these adhesions formed, but that they grow and develop to an extent which far surpasses their object. The appendix becomes enclosed and loses its mobility, the new attachments tending to fix it in a bad position. Hence, it is unable to rid itself of its fæcal and secretory contents.

Or, is this ready inflammation of the appendix due to infiltration of its numerous lymphoid corpuscles? The frequency with which phlegmasia of the other lymphoid organs, such, for instance, as the tonsils, occurs in thyroid inadequacy has already been pointed out.[1] Someone has said that the appendix is an abdominal tonsil. It is certain that appendicitis and tonsillitis are frequently observed in the same individual. A patient complains of severe tonsillitis; he is scarcely able to swallow his saliva. He is very surprised to discover that his appendix is tender on pressure, and he is even more surprised at being told that he is threatened with acute appendicitis. Sir Bertrand Dawson, physician to the London Hospital,[2] says that twenty years ago H. G. Sutton affirmed that tonsillitis and appendicitis readily occur in the same subject. "The truth of this was not then apparent to me, but Sutton's sayings have a wonderful knack of showing themselves true with the unfolding of the years, and I have satisfied myself there is sound clinical evidence for the existence of this association between inflammation of the tonsils and the appendix."

Among the disorders of the digestive apparatus in thyroid

[1] Végétations adénoïdes et myxœdème. *Bull Acad. Méd. de Belg.*, March 25th, 1898.

[2] The Microbic factor in gastro-intestinal disease and its treatment. *The Lancet*, April 29th, 1911, p. 1129.

insufficiency, mention must be made of rectal hæmorrhage, which sometimes assumes an alarming character. This is due, in part, to premature ageing of the rectal veins, and in part to defective coagulability of the blood. Hæmorrhoids are very frequent in the subjects of thyroid insufficiency; they are generally ascribed to constipation, which certainly aggravates, though it does not produce them.

THE URINARY SYSTEM.

The kidneys appear to suffer comparatively slightly from the effects of thyroid insufficiency. It is true that cases of transudation of albumen are not infrequent, but the albuminuria is very slight. The occurence of urinary casts is exceptional. The lesion is in no case very profound, for the albumen disappears after a few days' treatment.

The bladder is very sensitive to the effects of thyroid insufficiency. Owing to their ill-nourished condition, the infiltrated mucous membranes desquamate rapidly, and large clouds of pavement cells are seen in the evacuated urine. The bladder becomes very sensitive to the contact of the urinary fluid, and there is a constant desire to micturate. The greater number of the children and adolescents who are the victims of nocturnal enuresis are subthyroidic, the mother frequently showing unequivocal signs of thyroid insufficiency, such as migraine, constipation, menorrhagia, premature greyness, etc. Incontinence of urine is sometimes associated with rectal incontinence, which may even be diurnal.

These children sleep very heavily, and during sleep their temperature falls. They seem to be in a state of stupor. The ejaculator urinæ reflex responds too readily, before the higher nervous centres have been warned. Nocturnal incontinence generally disappears as the child grows up, though it has been known obstinately to persist. Even after cure, however, a certain tendency remains, and there is a large number of adult women who are the victims of pollakisuria.

THE SEXUAL ORGANS.

It is evident from the photographs which appear at the beginning of this article that, where the function of the thyroid

is appreciably reduced, the sexual organs do not develop. The photographs also show that if the organism is supplied with the requisite amount of thyroid extract, the deficiency in development is made good within a comparatively short time.

Cryptorchidism, both uni- and bi-lateral, is by no means rare. Where the thyroid function is slightly impaired, as in infantilism of the Lorain type, development of the genitals is invariably retarded, and in many instances it is permanently inhibited. Infantilism of this type is usually of congenital tubercular origin. Such children are slight and fragile, and have the thorax long and narrow. They are invariably small for their age. The tonsils are hypertrophied, and the pharyngeal cavity is choked with adenoid growths. There is tenderness in the neighbourhood of the appendix, abdominal pain, and habitual constipation with sudden attacks of diarrhœa. Abdominal section reveals the long, opalescent appendix, charged with fæcal matter in a semi-fluid or coprolithic state. As a general rule, it is fixed in a bad position by adhesions of varying thickness. Large ganglia are present in the peritoneum, while the cæcum is loaded and of a bluish colour.

In girls, the ovaries develop late. Menstruation does not make its appearance until the eighteenth year, and then sometimes assumes the unusual form of menorrhagia. Menorrhagia in virgins is an alarming sign, and one likely to lead the unwary astray. The uterus is small and infantile. The posterior wall develops slowly, sometimes leading to a very marked retroflexion. This backwardness in development is the outcome of thyroid insufficiency. It is generally believed that menorrhagia is the result of retroflexion ; this, however, is not the case. Retroflexion and menorrhagia are both referable to the same cause, namely, thyroid inadequacy.

In women of normal thyroid function, the catamenia are moderate, both in degree and duration, and they do not give rise to fatigue. In subthyroidic women, on the other hand, the discharge is prolonged, frequently ceasing for a day and beginning again, while the intermenstrual periods are briefer than the normal. The higher the degree of thyroid inadequacy, the greater the menstrual losses. The profusion of the

discharge is directly due to infiltration of the muscular element as well as of the intra-uterine mucosa, combined with a want of coagulability on the part of the blood. That an important rôle is played by muscular atony is very evident. The vaginal mucosa is infiltrated and soft, and suggests to the touch the beginning of labour.

The therapeutic significance of the above is considerable. Where menorrhagia is due to thyroid inadequacy, the best hæmostatic is, undoubtedly, thyroid extract.

The effect which marriage has upon the vitality of the thyroid gland is well known. From the outset, the gland undergoes hypertrophy—sometimes visibly so—and from this increased activity the subthyroidic woman derives immense benefit. At the end of a period, which is sometimes very short, the uterine retroversion is corrected. Should she become pregnant, the secretory activity of the thyroid gland is redoubled. Signs even of hyperthyroidism are not infrequently observed from within a few hours of impregnation. The face becomes drawn, the eyes brilliant and feverish, and there is an impression of sudden general emaciation. The hæmophilia disappears, menstruation ceases. It may happen, however, that the stimulating influence does not last. Menstruation reappears, and the fertilized germ is carried off in the flood. Herein lies the secret of the many abortions which are the tragedy of so many women's lives. And it is in cases like these that thyroid extract is able to render such signal service. By its aid, it is possible to bring to a successful issue a pregnancy, which would otherwise have suffered fatal interruption. The favourable activity of the stimulated thyroid persists during the entire period of pregnancy and lactation.

After confinement, the maternal system is suddenly relieved of an enormous tax, and becomes, in consequence, overcharged with thyroid secretion. A portion is directed to the mammary glands, where it provides for the appearance of the lacteal secretion. Positive experiments with animals in milk have shown that, when the daily output begins to decrease, a marked increase is effected by the administration of thyroid extract. Women with impoverished thyroids instinctively prolong the period of lactation beyond the physiological term.

After weaning, they again fall into their former condition of subthyroidism. That this is invariably so, is proved by the fact that the older classic authors included prolonged lactation among the causes of myxœdema. The reader will, doubtless, perceive where the error in this point of view lies, and will agree with the present writer that, in all such instances, a condition of subthyroidism existed before the occurrence of pregnancy. The thyroid stimulus ultimately weakens, the secretion of milk is diminished and finally ceases, and menstruation is re-established.

A second portion of the thyroid reserve, accumulated during gestation, is directed to uterine involution. The muscular fibres of the uterus undergo fatty degeneration and disappear. Moreover, the process of involution will be rapid in proportion as lactation—which is itself a manifestation of the abundance of the thyroid secretion in the blood—is active and well maintained. Gynæcologists know that the most energetic measure for promoting involution is the establishment of lactation.

Occasionally, a subthyroidic woman is encountered whose earlier pregnancies were well borne. Gradually, however, the thyroid gland becomes less sensitive to the demands made upon it by conception, with the result that miscarriages take place. As the years go on, the classic picture of chronic benign subthyroidism is evoked, the patient gradually becoming the victim of headache, neuralgic pain, loss of memory, dental caries, constipation, menorrhagia, pseudo-asthma, chilliness, a sense of oppression in response to slight effort, giddiness, noises in the ears, palpitation, etc. The larger the number of the pregnancies, the greater the tendency to hemorrhage in general. Infiltration of the uterine mucosa facilitates the slipping of the placenta, thus producing a predisposition to placenta praevia, both lateral and, though more rarely, central.

Ultimately, as the sequel to a life of ailments and discomforts, the menopause supervenes. Sometimes it comes late in life, as late even as 56 or thereabouts. In a few fortunate instances, the migraine and rheumatoid pains disappear, the general condition becomes improved, and a new life begins

for the unhappy victim of thyroid insufficiency. Earlier in this article I offered an explanation of this spontaneous amelioration. Such instances are, however, rare. In the vast majority of cases, the condition of subthyroidism persists and becomes intensified.

ÆTIOLOGY.

Heredity plays a considerable part in the ætiology of thyroid insufficiency. It is rare to come across a myxœdematous or chondro-dystrophic dwarf, an infantile subject of the Lorain type, or an obese child, whose parents, more particularly the mother, do not show signs of thyroid inadequacy. The indisputable proof of this fact, supplied by observations extending over a wide field, is the foundation for the clinical definition of benign chronic subthyroidism, as outlined in these pages. It is urged that in all cases of myxœdema, whether malignant or benign, attention should not be confined to the patient, but should be directed to all other members of the family, both ascendants and collaterals.

The subject shown in Fig. 52 (Plate XXV.) is of a pronounced myxœdematous type. The eyelids are infiltrated; he suffers from rheumatoid pain, perpetual chilliness, and unrelieved oppression. The cuticle is dry, senile, and lamellated, and the epidermis is fretted by fine transverse lines. The entire body is heavy, gross, and infiltrated with an œdema which does not pit on pressure. There is invincible somnolence, and mere existence is a fatigue. Under the influence of thyroid extract, the infiltration was rapidly absorbed. The weight fell from 12 stone 1 lb. to 10 stone 9 lbs., a loss of nearly 19½ per cent. The patient became completely cured, and for 15 years was able to devote himself to his occupations. I had completely forgotten him, when his history was recalled to my mind by his daughter, who came to consult me. She is shown in Fig. 53 (Plate XXVI.).

The patient (Fig. 53) states that menstruation has always been very profuse and exhausting. Her hair comes out in large quantities; she suffers from migraine and headache. To a close observer the face presents a slight puffiness. She is tired, harassed, and has an uncontrollable desire to sleep. She

is at present suffering from sciatic pain in the left leg. Her hands are cold, puffy, of a bluish-red colour, and in winter are covered with chilblains. Under the influence of thyroid extract in minimal doses, the puffiness of the face disappeared, and all the symptoms, including the sharp sciatic pains, became ameliorated. Had I not been acquainted with the father, it is possible that I might have mistaken the origin of the daughter's condition. My attention having been directed to the possibility of subthyroidism, diagnosis was easy.

Fig. 54 (Plate XXVI.) shows four stages in the development of a child suffering from marked arrest of mental and physical growth. The condition is one of true myxœdema. She is 8 years old, and her height is 34 inches in place of the normal 46 inches. Her weight is 2 stone 5 lbs. The facial expression is that of extreme thyroid insufficiency. The skin is of the characteristic amber colour, with red patches on the cheek-bones.

The dystrophic process has not attacked all the tissues with equal violence, the epidermis and its appendages being comparatively healthy. The eyebrows are well defined, the black hair is pretty and abundant, the teeth are sound—a very rare finding in a myxœdematous subject. The bony structure, on the other hand, has suffered considerably. The femurs are bowed and the tibias show advanced rachitic lesions. The feet are short and flat. The abdomen is enlarged, a characteristic sign in dystrophia strumipriva, and there is an umbilical hernia. The floating ribs have been dragged from their position by the forward trend of the abdominal walls. This is scarcely perceptible in Photograph *a*, but in Photograph *b*, which illustrates the condition after one year of treatment, the great reduction in the size of the abdomen renders it clearly visible. The intelligence is very undeveloped, but it is not extinct. The temperature is very low, even in summer. In winter, it becomes glacial, and there is no means of keeping the child warm. She has little appetite, and is obstinately constipated.

The origin of the condition is not far to seek. While carrying the child the mother had several severe attacks of malarial fever, and was obliged to leave the low-lying village near Antwerp where she was living. She was confined in the

town. Four years before taking up her abode in the low-lying district, she had given birth to a son, now 12 years of age. Although slight, thin and delicate, he is perfectly healthy. A second child died from an abdominal trouble at the age of 5 months. The third child is the present patient.

It has often been shown that true congenital myxœdema is the outcome of the superposition of two grave blemishes in the parents, such, for instance, as syphilis and tuberculosis, gout or diabetes and syphilis or tuberculosis, alcoholism and syphilis. I carefully examined this woman with the object of discovering the nature of the blemish which, in combination with malaria, was able to produce so great a degree of degeneracy in the fœtus.

She was the victim of terrible migraine; she was very constipated; the liver and gall-bladder were sensitive; menstruation was excessive; the entire muscular system was subject to rheumatoid pain, which became more intense in the cold weather. She was depressed, discouraged, and inclined to melancholia; her temperature was subnormal; sh was subject to frequent palpitation and sensation of oppression; the skin was pale yellow in colour, closely resembling that of the child; she complained of giddiness, noises in the ears, and specks before the eyes. In fact, she presented the entire symptom-complex, which, in another publication, I have described as characteristic of chronio benign subthyroidism.[1] Without being myxœdematous, the woman was obviously suffering from a degree of thyroid inanition. The other causative factor was supplied by the malarial poison. The mother being unable to supply the fœtus with the necessary amount of thyroid secretion, a cretin was born into the world.

W. rapidly improved under thyroid medication. Photograph *c* shows her at the end of the first year of treatment. She did not at first tolerate thyroid well. She vomited violently every morning, like a pregnant woman. I insisted, however, upon the continuance of the treatment. In the course of the first

[1] De l'hypothyroïdie bénigne chronique ou myxœdème fruste. *Bull. de l'Acad. de Belgique*, March, 1899, Vol. XIII., p. 231, etiam in *Nouvelle Iconographie de la Salpêtrière*, 12th year, No. 3, 1899. With 29 photogravures and 7 illustrations.

year, she grew about 5½ inches. The rachitic deformities, although they had not disappeared, were considerably improved. The enlargement of the abdomen had subsided. The umbilical hernia had closed. The expression of the face had become thoughtful and inquisitive. The neck had emerged.

The second year of treatment was less happy in its results. The child had whooping cough in a very severe form, and was ill for five months. Growth during the second year amounted to only 2 inches. Photograph *c* shows her at this stage. The lower limbs have straightened out, and all traces of rickets have disappeared. About this time the parents were very much disturbed by a difficulty in speech which the child had developed, and which they attributed to the treatment. I had already observed such a symptom occurring in other cases under similar conditions. The patient finds an enormous difficulty in the articulation of words, especially of the first syllable. He pants with open mouth in a convulsive effort very painful to witness. In the case of W., the difficulty gradually subsided as treatment progressed.

In the third year, she grew 2¼ inches.

The fourth year produced only moderate results, owing to the fact that the treatment was not regularly pursued, but was suspended for months at a time. Nevertheless, growth amounted to 1⅓ inches.

Having been seriously admonished, the parents were more conscientious with the treatment during the fifth year, and growth was vigorous. She grew 3⅜ inches. Photograph *d* shows little W. after five years of treatment. Her sum of growth is 15⅓ inches. The lower limbs are straight and graceful. The most practised eye would fail to detect in this child the faintest trace of thyroid insufficiency.

The history of this case confirms the view that I have long held, and frequently expressed, concerning the ætiological unity of certain morbid conditions usually referred to separate causes. Infantile obesity, rickets, infantilism of the Lorain type, achondroplasia, true myxœdema, arrested and retarded growth of congenital syphilitic, alcoholic, nicotinic, malarial or tubercular origin: all these affections, when traced to their ultimate cause, are the outcome of thyroid insufficiency. Syphilis, tuberculosis, chronic ill-health and malnutrition,

consanguineous unions,—all these are factors which react, in the first instance, upon the thyroid gland, and bring about changes in the nature of its secretion. Does not the complete disappearance under thyroid treatment of the rachitic lesions in this little girl point to the fact, that osseous dystrophia is due to aberration on the part of the thyroid gland? The thyroid secretion is, in its very nature, specific; it is incapable of affecting lesions which do not come within its scope.

To return for a moment to the child W.; her growth has progressed during the last three years, and her height is now 4 feet 9 inches. Fig. 55 (Plate XXVI.) shows her as she is to-day.

Now observe the portrait of the mother (Fig. 56, Plate XXVI.). The hair is of a magnificent silver-white. She is better than she was 14 years ago. She has passed the climacteric and the thyroid resources which, during her sexual life, were impoverished by the inhibition of menstruation, are now amply sufficient for the purposes of general nutrition. She still suffers, however, from rheumatoid pains and a sense of oppression. When the symptoms become acute she takes thyroid extract, which affords her relief.

Brissaud has stated that the thyroid gland is the most delicate and the most vulnerable of all the organs. All the more profound pathological influences—tuberculosis, syphilis, alcoholism, malaria, consanguinity, chronic malnutrition, excess and deprivation of every description—react upon its vitality. Up to the present, the stigmata of thyroid insufficiency have not generally been sought in the victims of tuberculosis, syphilis, and alcoholism; nevertheless, it is certain that they are there. Generally speaking, the acute syphilitic lesions are trophic in their nature, and it is incontrovertible that the descendants of syphilitic subjects invariably show the accepted signs of thyroid inadequacy.

In Fig. 1, a case of thyroid degeneracy of hereditary tubercular origin was shown. Fig. 11 shows a child whose father married shortly after having contracted syphilis. Fig. 54 illustrates the vitiating effect of malaria in the mother.

All infective diseases, the athrepsia of infants, measles,

scarlatina, whooping-cough, and acute articular rheumatism in particular, exercise an extremely deleterious influence upon the thyroid gland. When the gland is robust, it offers a certain resistance; when it is congenitally impoverished, there is disaster. In the majority of instances acute articular rheumatism forms part of the history of the victim of true myxœdema. I have, however, seen cases in which acute articular rheumatism made its appearance long after definite signs of thyroid insufficiency, such as metrorrhagia, were established. Under these circumstances, it is not possible to place the entire pathogenetic responsibility for thyroid inadequacy upon acute articular rheumatism. There is no doubt, however, that it is an aggravating factor in the condition. It may be conceded then, in the absence of more certain information, that acute articular rheumatism shows an undeniable predilection for subjects in whom the thyroid defences are weakened.

The work of Sir Arbuthnot Lane has already been mentioned in the course of this article. He believes that the toxæmia which results from chronic constipation, exercises a deleterious influence upon the thyroid gland, and of this point he is extremely tenacious. It has already been shown that chronic constipation is an inevitable outcome of dysthyroidic infiltration of the visceral muscles, in combination with poverty of the intestinal secretions. Once the toxæmia is established, a vicious circle is formed. The favourable influence, which marriage and pregnancy have upon thyroid insufficiency, has already been described. It is satisfactory to note that Arbuthnot Lane also advises marriage in the case of young persons suffering from intestinal stasis with consequent toxæmia.

The clinical factors of which a brief account has been given in these pages point to an extreme frequency on the part of thyroid insufficiency. For good or ill, we are the heirs of hundreds of generations, comprising thousands of individuals, who, in the struggle against pathological elements of various kinds, have suffered alteration of their thyroid resources. It may be safely affirmed that few families escape thyroid insufficiency in a more or less marked degree.

SYMPTOMATOLOGY.

The expression of thyroid insufficiency is diminution of the nutritional exchanges. All the tissues of the body are subject to processes of nutrition and combustion, and no tissue is able to escape the results of impoverishment of the thyroid gland. For this reason, the symptom-complex of myxœdema, whether malignant or benign, is very comprehensive and it affects, to a greater or less degree, every organ of the body and each specific function. A detailed account has been given of the results of infiltration upon the muscles, the central nervous system, the bony tissue, the glands, the mucous membranes, and the epidermis and its appendages. The derangements which take place in the great organic apparatuses, the gastro-intestinal, sexual, and nervous systems, have also been described. For this reason, it is unnecessary to enter further into the matter here. The numerous photographs accompanying this article will serve to familiarize the reader with the general appearances characteristic of thyroid insufficiency.

TREATMENT.

The main fact, that thyroid insufficiency is invariably accompanied by infiltration, must never be lost sight of. Under the influence of thyroid extract, the infiltrates are absorbed and the patient loses weight. The weighing-machine not only confirms the diagnosis, but it controls the conduct of the treatment.

Care should be taken to guard against the exhibition of thyroid extract in excessive doses; in other words, against the too abrupt withdrawal from the tissues of the fat, mucin, and other waste products by which they are distended. Over-rapid absorption is accompanied by pain in the muscles, ligaments, and joints, and this pain is sometimes more intense than that which obtained before treatment. The heart muscles are peculiarly liable to affection, a fact which is alarming to patient and doctor alike. Too drastic a treatment may provoke cardialgia and tachycardia which have all the appearance of hyperthyroidism.

Again, the sudden combustion of the infiltrated material

may effect an abrupt transition from a state of hypothermia to one of hyperthermia, thus conveying the impression of fever, the symptom being entirely due, however, to over-rapid oxidation. For both these reasons, courage to go slowly is essential. It is inadvisable for the patient to lose more than $3\frac{1}{2}$—$5\frac{1}{4}$ ozs. a day. Even in the case of severely myxœdematous adults, I never exceed a dosage of three 5-gr. tabloids (B. W. & Co.) in the day. In slighter cases, I give either one or two tabloids, according to the daily loss in weight. Children tolerate thyroid well, and one to two tabloids may be given daily without fear of evil consequences. They grow very rapidly under the treatment. As a general rule, a child in whom growth is arrested or very noticeably retarded, will grow as much as from two- to three-fifths of an inch a month.

The method is essentially palliative in its action, and should be continued over a long period of time—a lifetime, in fact. The permanent dosage should be half the amount of the initial dose, and both should be controlled by the weight. As soon as the œdema has completely disappeared, health is re-established. Assimilation and digestion become normal, and nothing will prevent the patient from putting on weight. This, however, is not a disquieting symptom.

It is expedient to accompany the exhibition of thyroid by a mild aperient, such as aloin or cascarine. Aloine Houdé is an excellent preparation, one pill of $\frac{1}{25}$-gr. being given each night. Liquid paraffin, which is a favourite method in England, is a valuable adjunct to treatment. The dose is about a tablespoonful night and morning.

The patient may eat everything, meat included. I always, however, advise that little sugar should be taken, and no alcohol in any form whatever. Cold baths and any kind of cold hydrotherapy should be absolutely forbidden. There is little wisdom in robbing the victim of thyroid inadequacy of heat; chilliness is his normal state. As a general rule, the infiltration of true myxœdema disappears within sixty days.

Briefly, then, the rational method consists in the exhibition of thyroid extract in small doses; close attention to the weight and the régime; and perseverance in the face of muscular and nervous cardiac pain, should such arise.

The results of treatment are of a nature to convince the most sceptical. Nothing is more striking than the return to health of a victim of grave myxœdema. The hair grows, the expression becomes intelligent. In children, the increase in height is very striking. In women, the derangements of sexual activity are corrected, menstruation assumes a normal character, and the tendency to abortion disappears.

I have purposely refrained from discussing the other opotherapeutic measures, which are sometimes employed in combination with thyroid extract. It is essential in the first instance, to obtain an exact estimate of the value of thyroid extract alone. Later on, variations are permissible. Other opotherapeutic extracts, such as ovarian, testicular, suprarenal, and pituitary, are still very uncertain in their action. I am convinced that the best method of stimulating the ovary, testicle, suprarenal, and hypophysis is by way of the thyroid, which governs and controls all the internal secretory organs.

ENDEMIC GOITRE.

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On Deputation in connexion with the Study of Goitre and Cretinism in India, Central Research Institute of India, Kasauli.

(With Plates XXVII.–XXXII.)

WITHIN recent years the many theories as to the causation of endemic goitre have been narrowed down to those which attribute it to chemical ingredients of drinking water, to geological peculiarities of the soil imparting to the water a specific colloidal poison, to faults of nutrition, and to living micro-organisms. In a brief article, such as the present, it is impossible to enter into a discussion of the various arguments for and against these different views. The problem was fully discussed, with respect to the evidence available up to the end of the year 1912, in the Milroy Lectures for the year 1913.[1]

Since then a large amount of additional experimental and epidemiological research has been carried out, which has definitely demonstrated that neither chemical constituents of the water, geological peculiarities of the soil nor factors of nutrition are primarily responsible for the genesis of this disease. Its infectious nature is now generally admitted by the majority of those who have devoted special attention to its experimental and epidemiological study. I propose, therefore, in the present article to limit my account of endemic goitre to a summary of the facts which are known to us up to the date of writing (July, 1914), and to refer the reader to the original records of experimental and other researches for the proofs of these facts.

ENDEMIC GOITRE.

Synonyms.—Struma, wen, Derbyshire neck, Nithsdale neck, bronchocele, endemic thyroidomegaly.

Definition.—A chronic infectious disease occurring in more

or less circumscribed areas and characterized by a non-inflammatory and progressive enlargement of the thyroid gland, which is unattended by appreciable functional disturbances. It is due to the presence in the alimentary tract of certain undetermined organisms, whose toxic products reach the blood-stream and induce in the thyroid gland hypertrophic, hyperplastic, and degenerative changes. Acting through the medium of the maternal blood, these toxins may cause hypertrophy and hyperplasia, or fibrosis and atrophy of the fœtal thyroid, thus giving rise to congenital goitre or to the varying degrees of cretinism.

Prevalence.—The extent to which goitre prevails in European countries generally and in the East is seldom appreciated. In France, Germany, Austria, Switzerland, and Italy large numbers of conscripts are annually exempted from military service on account of goitre. Baillarger estimated that, about the year 1874, there were in France alone no less than half-a-million goitrous persons and 122,700 cretins and cretinous idiots. The disease is probably less prevalent now-a-days than formerly, but it still gives rise to an immense amount of disability in almost every country in Europe. In India, at the present time not less than five million persons are afflicted with goitre, while half-a-million is a low estimate of the numbers who suffer from its congenital manifestations.

Prevalence in Animals.—In endemic localities, goitre may be met with in domestic animals and birds. It occurs in mules, oxen, horses, dogs, cats, goats, pigs, sheep, white rats, white mice, and in fowls and pigeons. It occurs also in artificially-bred fish, especially in trout, which are often very severely affected (Fig. 1). In animals living in the wild state, the disease is infinitely less common, and is generally to be found only in those whose habits of life have to a considerable extent been modified by the vicinity of man and his domestic animals. Thus, it is excessively rare in wild rats, although under certain conditions of life it may be very prevalent amongst tame rats.

Although fish of carnivorous habits, such as the pike, are more subject to goitre than are others, their susceptibility to it appears to vary greatly. Certain species of the Salmonidæ have an almost complete natural resistance to the disease[21];

amongst susceptible species certain batches reared in captivity show a high degree of immunity.[21]

Congenital goitre commonly occurs in the offspring of goitrous animals (Fig. 2), and so-called "epidemics" of goitre among domestic animals and artificially-bred fish[21] have frequently been reported. Amongst animals, as amongst men, those that are well cared for are much less liable to suffer from the disease.

Geographical Distribution.—Endemic goitre is widely distributed over the whole world. Few countries appear to be entirely free from it. It is so common in certain parts of England and Scotland as to be distinguished by the names: "Derbyshire neck" and "Nithsdale neck." It is most prevalent in temperate and sub-tropical zones. It is found, however, in regions of great cold, as in parts of Siberia, in Finland, and in the Hudson Bay Territory of North America. It occurs also in regions of great heat, as in tropical South America, Borneo, Sumatra, Java, India and Ceylon. While, therefore, temperate and sub-tropical climates are more favourable to its development, neither great heat nor great cold excludes its occurrence.

Orographical Distribution.—The association of the endemic with mountainous regions is one of its most striking peculiarities. The Alps, the Pyrenees, the Carpathians, the Himalayas, the Caucasus, the Andes, the Cordilleras, the Ural and Altai Mountains, and, in our own country, the valleys of the Pennine range, the Cotswolds, and the Mendips, are all noted haunts of goitre. But while it is true that the disease has its home in the mountain ranges of the world, it is not confined to them. It occurs in the plains of Lombardy, of Piedmont, of Alsace; in the plains of the Lena and Obi in Russia; of the St. Lawrence, in Canada; of the Ganges and the Brahmaputra, and of the Chenab and Sutlej in India.

Some mountainous countries, on the other hand, are almost exempt from goitre, as, for example, certain parts of Norway and the Highlands of Scotland, where it appears to be almost unknown. Although the hilly nature of a country cannot be regarded as a necessary factor for the development of goitre, there is considerable experimental ground for the belief that its preference for mountainous regions may, to

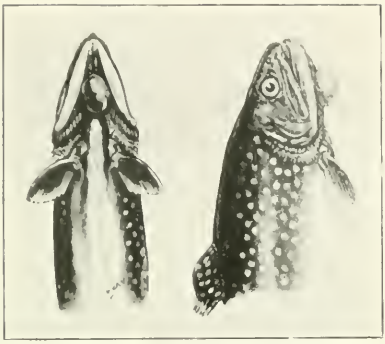

Fig. 1.—*Goitre in artificially-bred trout (Dr. David Marine, Cleveland)*

Fig. 2.—*Large congenital goitre in prematurely born goat (Experimentally produced.*

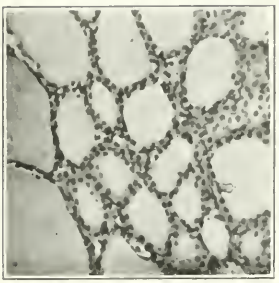

Fig. 3.—*Normal thyroid gland of rat; colloid or resting type.*

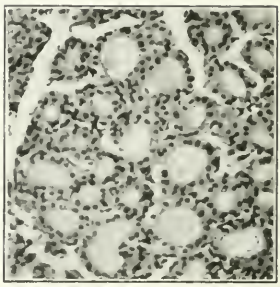

Fig. 4.—*Normal thyroid gland of rat; actively secreting type.*

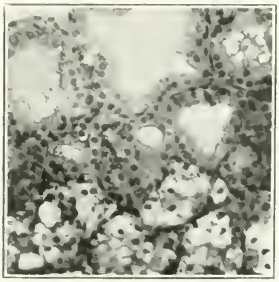

Fig. 5.—*Goitrous thyroid gland of rat; note columnar epithelium, absorption of colloid and degeneration of parenchyma cells.*

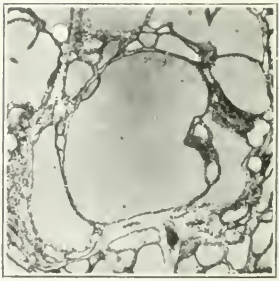

Fig. 6.—*Normal active; note evidences of previous hyperplasia, irregularity in shape and size of vesicles and their distension with colloid. Low power.*

some extent, be dependent upon the increased functional activity of the thyroid gland, which residence at high altitude often entails.[2]

The marked association of goitre with rivers, canals, and irrigated or marshy tracts is another noteworthy feature of its distribution. This association is especially obvious in India and Burma, where the disease is markedly prevalent along the course of such great rivers as the Brahmaputra, the Ganges, the Indus, the Chenab, the Sutlej, the Irrawaddy, and the Salween. Even in localities where goitre is rare, as in parts of Madras, such rivers as the Godavari, the Kistna, and their tributaries, may be associated with goitre in their upper reaches. It also occurs very commonly along the course of canals and in irrigated and marshy areas. A notable example of the importance of the marshy nature of the soil is afforded by the districts north and south of the river Ganges. In the marshy lands north of the river, goitre is excessively common; in the less extensively inundated lands south of the river, it is comparatively rare. Similar observations have been recorded in Austria and Silesia.[3]

Altitude.—Goitre is found at all heights above sea-level where man can live and cultivate the ground. It is to be met with in the Himalayas at all altitudes up to 10,000 feet. On the other hand, it is not absent from the sea-coast, as is often erroneously stated. It occurs in the delta of the Ganges, in the island of Cutch, on the coast near Manilla Bay, in the island of Arran, in Algeria, on the shores of the Mediterranean Sea, and on the shores of the Bury estuary in Glamorganshire.

Seasonal Prevalence. — Goitre exhibits a definite seasonal prevalence, which is generally constant for any given place, but may vary in different localities. In certain parts of Himalayan India, which are not reached by the monsoon, new cases of goitre arise and enlargements of pre-existing goitres take place during the spring and, less commonly, during the autumn months. At other seasons of the year, it is much less liable to develop.

In Himalayan localities which are reached by the monsoon, the rainy season is especially favourable to the development of the disease. The seasonal prevalance of goitre is probably dependent to some extent upon the seasonal variation in the

iodine content of the thyroid gland; this is at its lowest ebb during the first four months of the year.[4] In European countries, where endemic goitre is supposed to originate most commonly in the months of March, April, May, and June, the disease is sometimes called "summer goitre" or "goitre aigu." Many examples of so-called "epidemics" of goitre occurring at this season are to be met with in the literature.

Epidemic Goitre.—The most striking feature of these "epidemics" is that they arise only in endemic centres, in the neighbourhood of such centres, or in localities where the disease has previously been prevalent. They occur usually amongst susceptible newcomers to an endemic area; consequently, school children and young soldiers, especially if they are living in badly ventilated or unhygienic schools and barracks, are especially liable to be attacked. There is no essential difference between epidemic and endemic goitre.[1]

Behaviour of the Endemic.—The endemic prevails especially in rural districts. Although it may be comparatively common in many towns, as, for example, in Innsbrück, Vienna, Bern and Bayreuth, and in Muzaffarpur in India, it is never found to prevail to such an extent as in country districts.

The endemic prevails with different degrees of intensity in different countries and in different parts of the same country. In some, the endemicity is very high; in others, "it is so widely spread over the whole country, while at the same time it is so slight, that it easily escapes notice, and cases of goitre are often considered to be sporadic, which should more correctly be classed as endemic" (Berry). Thus, while the degree of endemicity varies, it would be difficult to declare any area to be wholly goitre-free.

Endemic Goitre is essentially a Place Disease.—In any locality in which the endemic is well-marked, as in the Alps and Himalayas, it will be found that it prevails with widely different degrees of intensity in villages situated adjacent to one another. Even in a goitrous village, occupants of certain houses, groups of houses, or institutions, may escape the disease, or suffer from it in such slight degree that it is not noticeable. This limitation of the malady to certain places is well brought out by recent experimental[5] and epidemiological work,[27] which has demonstrated the great importance of room,

house, or place infection in the genesis of goitre.

In an endemic area, the disease may fluctuate, and is subject to periods of increase and decline. It has made its appearance in many places where it was formerly unknown, and has disappeared partially or wholly from others.[1] It seems probable that a degree of immunity to the disease may gradually develop in certain communities.[24]

ÆTIOLOGY.

Race.—All races of mankind suffer from goitre, for there appears to be no such thing as race immunity to the disease. Among animals, some species of fish appear to be very resistant to it.[21]

Heredity.—It is extremely doubtful whether heredity plays any part in the ætiology of goitre. The same exciting causes which produce the disease in the parent produce it also in the fœtus and the child; a congenital instability of the thyroid mechanism, due to the action of goitrigenous toxins on the fœtal gland, is present in a considerable percentage of all children born of goitrous mothers. Such children are, consequently, more apt to become goitrous in later life than those whose mothers are goitre-free. Succeeding generations, under continuous goitrous influences may, however, develop some degree of natural resistance to the disease ([21], [24]).

Predisposing Factors.—Persons of a lymphatic temperament, and those of a neurotic constitution, appear to be especially prone to develop goitre.[6] Newcomers to an endemic area are very susceptible to it; but this susceptibility tends to diminish with increasing age. Other important factors, which favour in greater or lesser degree the development of goitre, fall into three main classes: (1) those which impair the functional activity of the thyroid gland, (2) those which make undue demands upon its functional powers, and (3) those which favour the entry of the excitant or excitants of the disease into the body.

Amongst factors which may be included in the first class are attacks of certain infective diseases, notably: rheumatism, rheumatoid arthritis, malaria, measles, intestinal disorders and helminthiasis. The causal agents of these conditions, or their toxic products, are all capable of inducing hyperplastic and

fibrous changes in the gland.[7],[8] Amongst factors which impose an added strain upon the functional powers of the thyroid are residence at altitudes considerably above that of sea-level,[2] defective air space,[9] improper food or defective food supply,[10] puberty, sexual activity, menstruation, pregnancy and emotional states, such as fright and continued mental strain. Under all these circumstances, it is the accumulation of demand in the presence of the excitant of goitre which determines the enlargement of the thyroid gland. Amongst those factors which favour the entry of the excitant or excitants of the disease into the body, are unhygienic conditions of life, residence on damp soil, and an occupation or social status which involves close and continued contact with infected soil. It is for this reason that goitre is much commoner amongst the labouring classes and in rural districts than amongst other classes of the community or residents in towns.[28]

In addition to these factors, there are others which favour the action of the excitant of the disease after its entry into the body. Some of those which have already been mentioned act also in this way; intestinal disorders are of especial importance in this connection. The use too of waters of a high degree of bacteriological impurity, of very hard waters, or of waters holding much mineral matter in suspension favours the onset of goitre, probably by producing abnormal states of the intestinal mucosa.

Age.—In certain regions, where the endemicity of goitre is high, the disease is not uncommonly met with in breast-fed infants. In these cases, it is congenital. Recent research has shown that congenital goitre occurs, under experimental conditions, in 63 per cent. of the offspring of goitrous rats.[11] Under similar conditions, the offspring of goitrous goats are often born with goitres of large size (Fig. 2, Plate XXVII.). In regions where goitrigenous influences are not so potent, congenital goitre is less commonly seen. Congenital goitres are usually uniform enlargements of small size, which tend to disappear spontaneously a few months after birth.

The incidence of the disease in children varies in different endemic areas, and appears to be dependent in considerable measure on the duration of the endemic in any given locality,

and upon the degree to which a natural resistance to the disease has been evolved among the indigenous inhabitants. In some regions, where goitre has prevailed for centuries, visible goitres are comparatively rare in indigenous children below the age of eight years. In others, where the disease is of more recent introduction, its incidence in children of all ages is often very high, and in a locality where it is beginning to prevail cases are to be found chiefly amongst the children.

When children are subjected to goitrigenous influences for the first time, they are markedly more susceptible to the disease than are adults.[1] The most susceptible age is nine years in the case of boys, ten years in the case of girls.[2] After the age of ten, the susceptibility diminishes slightly and again increases with the onset of puberty, a circumstance which is especially notable in the case of girls. With increasing age, the susceptibility gradually diminishes in the case of males, but increases in the case of females during the child-bearing period of life.[1]

Sex.—Up to the age of puberty, goitre affects the two sexes almost equally; it is, if anything more common in girls. From the age of puberty onwards, females are much more liable to suffer than are males. The sex incidence is, however, very variable in different districts, and is dependent largely upon the severity of the endemic. Where the endemicity is slight, cases may be met with only amongst women[1]; but in regions of high endemicity, the proportion of men to women affected may approximate as closely as one to one.[1]

The influence of the child-bearing period of life on the development of goitre is very great. In localities where goitre is not supposed to be endemic, as, for example, in London, the thyroid gland enlarges as a consequence of pregnancy in a little less than 50 per cent. of all cases.[12],[13] The added strain of goitrigenous influences greatly increases this proportion, and converts these physiological swellings into pathological.

Influence of Length of Residence in a Goitrous Locality.—Goitre may develop in as short a time as ten days after exposure to goitrigenous influences; this is exceptional.[1] Amongst young susceptible newcomers to a goitrous district, a considerable

proportion of cases develop within six weeks to three months after their arrival. The liability to the development of the disease increases with length of residence in an endemic centre, and after a period of residence of eight years in such a centre the majority of young people become goitrous.[2] Goitre shows a marked tendency to disappear when the sufferer leaves the goitrous district; it almost invariably reappears in such persons when they return to the infected locality.

The Infecting Agent or Agents of Goitre.—It has been shown that goitre is essentially a place disease, and that it is intimately associated in its origin with dirt. The organisms which are capable of causing it live in the soil of infected localities, and particularly in soil which contains a high proportion of organic matter of human or animal origin. They are present especially in and around filthy human and animal habitations; they cling to certain houses, rooms, stables, byres, animal cages, or fish-tanks, in which the excrement of the inhabitants is allowed to accumulate. They are capable of life in waters which are grossly polluted and show a high bacterial content,[2] but in pure water or in water exposed to the purifying influences of sedimentation, oxygenation, and sunlight their life is comparatively short, and their powers of multiplication very limited.[14]

These organisms reach the alimentary tract of man and animals by means of infected soil, food, or water, and there they flourish and produce toxins which, on absorption into the blood stream, initiate the goitrous changes in the thyroid gland.[15] Soil[1, 16, 27], water[1, 2], and food are, therefore, vehicles only whereby the infecting agent or agents reach the body of men and animals. It seems almost certain that the great source of the disease is the infected individual, and that he is the producer, the reservoir, and the distributor or "carrier" of the infecting agents.[5] These agents are discharged from the body in the fæces,[5] and it may be in other ways not known to us, as, for example, in the urine and saliva. If they reach a damp soil containing a high proportion of organic matter they live, and it may be multiply; while if they reach an organically impure and stagnant water which is protected from the purifying effects of light and air, as in the case of many wells ("goitre wells"), they may survive for a considerable time.

All the evidence at present available points to these as the

common modes of infection; but there may be other means, whereby the living excitants of the disease are conveyed from the sick to the healthy. It is possible, for example, that flies may act as conveyors of the infection to man, or that certain ecto-parasites may be concerned in its transmission; there is, however, no evidence at present available to suggest that any ecto-parasite or biting insect acts as a host for the further development of the living excitant of endemic goitre outside the body of man and animals[2, 5]. The very wide distribution of the disease in the animal kingdom renders such a mode of spread improbable. In their manner of origin and spread, endemic goitre and typhoid fever closely resemble one another. The conditions which are favourable to the development and spread of the one are equally favourable to the other.

The evidence, provided by the recorded results of experimental research, appears to warrant the belief that the causal agent or agents of goitre are facultative anærobic organisms, probably bacteria, inhabiting the intestinal tract; it does not, however, permit of a more definite conclusion as to the nature of these agents[1, 5].*

HISTO-PATHOLOGY OF GOITRE.

The histological characters of the normal thyroid gland vary within wide limits, and are dependent upon its state of physiological activity. This state is influenced greatly by such factors as food, age, sex, pregnancy, bodily health, season, and altitude.[18] The thyroid glands of the majority of healthy animals living at sea-level or at altitudes up to 1,000 feet above sea-level are in the "colloid or resting state," that is to say, their vesicles, which are uniformly circular or oval, are filled with normally staining colloid, and are lined by

* In a recent issue of the *B. M. Journal* (July 18, 1914) Mr. Farrant has sought to prove that the causal agents of endemic goitre are atypical forms of *Bacillus Coli Communis*. The experimental observations which he has recorded do not, in my opinion, justify this conclusion. While it has long been recognized that bacteria of this group are capable of causing marked histological changes in the thyroid gland—a property which they share with certain other intestinal bacteria and parasites—it has not so far been demonstrated that they are capable of causing *enlargement of the thyroid gland*, i.e., *goitre*. I have been unable to produce *goitre* in white rats—which are very susceptible to the disease—by feeding them daily, and for a period of over ten months, on coliform organisms isolated from a water credited with goitrigenous properties.—R. McC.

flattened or low cuboidal epithelium. The intervesicular tissue and stroma are scanty (Fig. 3, Plate XXVIII.).

At certain seasons of the year, with impairment of bodily health, with defective or inappropriate food supply, in consequence of residence at altitudes considerably above sea-level or from other causes, the thyroid may assume the characters of the "actively secreting gland," that is to say, the blood supply to the organ increases, the vesicular epithelium becomes cuboidal and vacuolated, the stored-up colloid undergoes absorption and a thin pale staining colloid is exuded from the secreting cells (Fig. 4, Plate XXVIII.). There is no increase of the stroma, but the intervesicular tissue may appear relatively increased in amount owing to the emptying of the vesicles of their colloid contents; this is especially noticeable as an effect of starvation.[18]

The histological changes peculiar to simple goitre indicate an exaggeration of the normal physiological process of secretion. So gradual is the departure from normal in some early cases of the disease, that the histological evidences of pathological change are often extremely slight. The line of demarcation between the normal physiological and the pathological states is consequently somewhat arbitrary.[18]

The goitrigenous process affects the whole organ and results in the formation of a "struma parenchymatosa diffusa." The earliest changes to which it gives rise consist in: (1) the congestion of the gland; (2) the vacuolation and absorption of the stored-up colloid; (3) an increase in height and in the number of cells lining the acini—these cells may become columnar or high columnar; (4) an increase in thickness of the acinar walls; (5) a multiplication of the intervesicular cells; (4) the formation of many new vesicles; (7) diminution in size of the vesicles—owing to the preceding changes; (8) the protrusion of the acinar walls, in the form of "buds," into the vesicles; (9) the production of new colloid which is formed partly by the discharge of a thin secretion from the heightened epithelium, and partly by the shedding into the vesicles of portions of the vesicular cells themselves; (10) a moderate desquamation of the vesicular epithelium; (11) an increase of the fibrous stroma of the gland; (12) degenerative changes in the parenchyma cells; and (13) sclerotic

changes in the vessel walls (Fig. 5, Plate XXVIII.).

The process which results in these changes may be acute, much more commonly, however, it is gradual and chronic. The histological picture varies considerably in different cases, according to whichever of these changes may predominate. Thus, in some, the intervesicular or stroma hyperplasia may be the more pronounced; in others, hypertrophy and hyperplasia of the vesicular epithelial may be more marked. Different parts of the gland may be affected in varying degrees, and may exhibit varying pictures, according to whether the process is advancing or receding; as a rule, however, the whole organ is uniformly affected. These changes usually result in an increase in size of the organ, but pronounced hyperplasia may be present in glands which are not enlarged, or only slightly so.[18]

The process results in an increase of the secretory surface of the organ. The increase of the fibrous stroma and the degenerative changes in the parenchyma cells, which occur *pari passu* with the epithelial proliferation, are the consequences of the abnormal activity, as well as of the action of the toxic substances initiating it.[18]

It is amply proven that the changes, which are characteristic of the earlier stages of goitre, are due to the action of toxins and not to the presence in the gland of living organisms.[1], [7] The goitrous thyroid of endemic localities is invariably sterile. The action of these toxins is an *intermittent* one, so that the process periodically abates, and the gland then reverts —scarred, it is true—to a state of rest, in which the colloid secretion is again stored up in the vesicles. Repeated attacks, however, such as occur in endemic centres at certain seasons of the year, result in further multiplication of the parenchyma cells and of the acinar units, as well as in the further increase of the connective tissue stroma. Thus, a stage is ultimately reached when the secretion is not only produced in increased amount by the increased number of the acini, but finds it less easy to escape therefrom, owing to the very considerable increase of the fibrous stroma in the goitrous gland.

Alternating periods of hyperplasia, and of reversion to the "colloid state," result in the damming up of the secretion, and in great distension of both recently-formed and old vesicles. This distension of vesicles of all shapes and sizes with thick,

tenacious colloid is a condition invariably exhibited by such chronic goitres when removed at operation (Fig. 6, Plate XXVIII.). In all chronic goitres, considerable atrophy of the parenchyma cells ultimately occurs, and the functional activity of the gland *for each unit of space* becomes diminished. Degenerative changes, cystic and tumour growths, add further variety to the picture, but these are complications implanted on the initial process.

Owing to the intermittent action of the goitrigenous toxins, the functional powers of the thyroid never become so impaired as to cause pronounced symptoms of hypothyroidism. In Graves's disease, on the other hand, the goitrigenous toxins are *continuous* in their action; consequently, fibrosis of the gland and pronounced atrophy of its parenchyma cells, with resultant myxœdema, are not uncommon sequelæ of this condition.[18]

SYMPTOMS AND COURSE OF THE DISEASE.

The goitre, which is soft in consistency, is, as a rule, a uniform enlargement, though occasionally one or other lobe may be the more prominent. In the latter case the more prominent lobe is usually the right. There is not infrequently considerable pulsation in the vessels of the neck. The swelling does not, as a rule, progress in size in a uniform manner, but varies considerably from time to time. It may even disappear for a time only to reappear again at a later date. Goitres at this stage are rarely large. The swelling is unattended by symptoms, other than the subjective sensation of fullness in the throat. The enlargement, after attaining a certain point, usually subsides to a size at which it remains stationary.

Spontaneous recovery, while the patient continues to live in the endemic area, is not uncommon. It has been found to occur in 11 per cent. of cases in boys and in 7 per cent. of cases in girls of the Lawrence Military Asylum at Sanawar.[2] Spontaneous recovery appears to confer a degree of immunity against recurrence.[21] Incipient goitres very commonly disappear spontaneously when the patient leaves the goitrous locality. Such a train of events is what may be called a "first attack" of goitre. The tendency is for the gland to revert to a condition approaching as nearly to

normal as is possible. In some few cases the reversion may be complete, but in the great majority the "attack" leaves the thyroid larger than it found it.

The immunity which is probably conferred by such an attack of goitre is of a very transitory character; with succeeding springs and autumns, in parts of Himalayan India, recurring attacks of thyroid hyperplasia occur, and the gland increases in size by a step-like process, which was also described by Lawson Tait in the case of goitre associated with pregnancy. The process is comparable to that which takes place in the spleen, as a result of successive attacks of malaria. If the patient is subjected to goitrigenous influences for any length of time degenerative processes soon make their appearance, and the large cystic and adenomatous goitres which are so common in goitrous localities are the result. Should the subjection to goitrigenous influences be intermittent, the onset of degenerative processes is much longer delayed and these changes are much less marked than in the case of persons who constantly reside in a goitrous locality.

Symptoms referable to disturbances of the function of the thyroid are almost completely wanting in endemic goitre. In long-standing cases, in which considerable degenerative change has occurred, slight symptoms of hypothyroidism may occasionally be observed. Tetany is not uncommon in certain parts of the Himalayas among women suffering from such goitres.[29] Such symptoms as occur are mainly referable to the effects of pressure on the important structures in the vicinity of the gland. Respiratory disturbances may be present, and are due to mechanical constriction of the trachea, more rarely to mechanical injury to the nerves of the larynx.

Functional disturbances of the heart, resulting in dilatation and hypertrophy of the right heart, may be due partly to mechanical impairment to the venous circulation (Rose's goitre heart), partly to hindrance of respiration (Kocher's goitre heart with dyspnœa), and perhaps also to compression of the cardiac nerves.[19] Bircher has attributed to the toxic agents of endemic goitre a definite action on the heart, which results in its enlargement and in an increase in the

thickness of its walls.[20] A considerable experience of endemic goitre in India and Europe, however, leads me to believe that the heart is not affected in simple goitre, except as a result of the mechanical effects of the enlarged thyroid. When an apparently simple goitre is associated with cardio-vascular symptoms, however slight, and which are not due to the effects of pressure, the condition is probably one of incipient Graves's disease.

THE BLOOD IN GOITRE.

Blood changes of a fairly definite character occur in endemic goitre. The number of erythrocytes is diminished, as well as the hæmoglobin index. The coagulibility of the blood is increased. The total number of leucocytes is reduced. The polymorphonuclear leucocytes are constantly below normal limits; the absolute reduction in their numbers may be 50 per cent. of the normal. They may form as little as 30 per cent. of the leucocytes in peripheral blood; the average differential count in 73 cases was 46·5 per cent. The small mononuclear cells are usually above normal limits; the absolute increase in their numbers may be twice that of the normal. In differential leucocyte counts, they may form as many as 45 per cent. of the total leucocytes in peripheral blood; the average count for 73 cases was 32·2 per cent. The eosinophile cells are usually increased in numbers, and may form as high a proportion of the total leucocytes in peripheral blood as 20 per cent.; the average count for 73 cases was 10 per cent. The large mononuclear cells are usually within normal limits.[1]

The blood changes of exophthalmic goitre resemble those of endemic goitre, in that the polymorphonuclear cells are diminished, and the mononuclear cells are increased in numbers. *There is, however, no blood-picture which can be said to be characteristic of either Graves's disease or of simple goitre,* so that the employment of the so-called "blood-picture test," in the differentiation of cases of simple goitre from atypical cases of Graves's disease, is valueless and calculated to lead both to errors of diagnosis and to the adoption of surgical methods of treatment, which are not justified by the gravity of the patient's condition.

No organisms of a bacterial or a protozoal nature, which can be considered as causal agents of the disease, have been found in the blood or thyroid glands of cases of endemic goitre.

PROPHYLAXIS.

Goitre is mediately infectious but non-contagious. Man and his domestic animals are the great source of the disease, their habitations are centres of infection, and all food materials which directly or indirectly have been fouled by their excreta may be vehicles for its spread. Contact with the infected individual is of importance, in so far as it affords opportunities for the transference of the infecting agents from the sick to the healthy. Soil and water are the main vehicles whereby this transference is effected, and their influence in this connection has been abundantly shown by experiment [1], [16], [21]. Infected soil is the more important of the two, since the life of the infecting agent is probably much longer in damp and organically polluted soil than in water; it is from the soil also that a water derives the noxious agents.

It is very necessary, therefore, to avoid contamination of the hands and of the food by the soil of infected localities. Food should be protected from flies, and should be prepared by non-goitrous persons of cleanly habits who, presumably, are not "carriers" of the infection. Drinking water should be sterilized by boiling or by such chemical agents as chlorine or iodine. That the importance of this measure is great is shown by the fact that the addition of perchloride of mercury (1–4,000,000) to the water in which trout are artificially reared effectually prevents and cures the goitre from which these fish are so liable to suffer.[21] In some localities, the consumption of certain waters appears to prevent the development of the disease; these waters usually contain small amounts of iodine, and are of a high degree of bacteriological purity.

The improvement of personal hygiene, the provision and maintenance of sanitary dwellings and of pure and well protected water supplies, the institution of hygienic systems of conservancy, the proper disposal of sewage, the removal of the stables and byres of domestic animals to a considerable

distance from human habitations, the abolition of cess-pits and of manure heaps in the immediate vicinity of dwellings are measures which will result in the diminution or disappearance of the disease in all goitrous localities.[1]

TREATMENT.

The treatment of goitre depends upon the stage to which the disease has progressed. Medicinal measures are applicable only to cases of comparatively recent origin ; when secondary degenerative changes—cysts, adenomata, fibrosis, and calcification—have become ingrafted upon the initial process of thyroid hyperplasia, medicinal treatment is of little or no avail, and the case must be dealt with by surgical means. It is with the non-operative treatment of goitre that I propose to deal.

When goitre has developed in a locality where the disease abounds, cases of recent origin and of small size, especially in young people, usually disappear spontaneously when the patients are removed to a non-goitrous district. Residence at the sea coast is often of considerable curative value in such cases. It is to be remembered that persons who have once suffered from goitre are prone to a recurrence of the swelling, should they again reside in a goitrous district. Change of residence, however, is a measure which is not practicable in the majority of cases. Under such circumstances, treatment should be directed to the removal of the exciting cause of the disease, and of the factors which favour its action.

In dealing with the exciting agent or agents of goitre it is necessary (1) to prevent their entry into the body, and (2) to destroy or diminish the number of those which already exist therein. We must, therefore, correct all unhygienic conditions of life, advise the use of boiled water or of water which has been sterilized, and instruct the patient to avoid the contamination of the food by soil-infected hands. Of remedies which may be employed to destroy or to reduce the numbers of the goitrigenous organisms in the alimentary tract, the most important are the antiseptics—iodine, thymol, salol, β-naphthol, quinine, hydrofluoric acid, the bacillus bulgaricus—and vaccines.

Iodine is the most potent of all known remedies in the treatment of parenchymatous goitre. It is best given in the

form of the tincture, either alone or combined with iodide of potassium. The drug must be administered in sufficiently large doses to be efficacious. Five minims of the tincture, combined with five grains of the potassium salt, is a suitable initial dose. This may gradually be increased till the patient is taking three or four times as much (30); care must be taken to stop the administration of iodine, if symptoms of iodism are produced or if the digestion is upset. It is to be remembered that the indiscriminate use of iodine may precipitate the onset of Graves's disease ("Iodine-Basedow" of German authors). It should not, therefore, be administered in cases in which cardio-vascular symptoms, however slight, are present. When prescribed in suitable doses, its effect on parenchymatous goitres is obvious within a month. If it produces no good effect in this time, its continued use is not likely to be beneficial.

Iodine may be applied externally over the enlarged thyroid, either in the form of the biniodide of mercury ointment, or of the tincture. The ointment is much used in India, where the patient is instructed to rub it well into the neck, and to sit exposed to the sun for one or two hours. A few such applications often result in marked reduction in size of the swelling. The external application of iodine is a useful adjunct to other forms of medication.

Intestinal Antiseptics.—Of these the most potent is *thymol*.[1] It is given in doses of 10 grains night and morning, and is best administered in the form of a coarse powder, washed down by a draught of water. The bowels should be kept active by the occasional use of salines, and *all solvents of the drug must be excluded from the dietary*. In recent cases of the disease, the beneficial effects of this drug are often very striking. The dietetic restrictions attending its use make it more suitable for cases of the disease amongst Indians than amongst Europeans. In the latter, *salol* or *β-naphthol* are more convenient, but less efficient remedies. They may be administered in full doses twice daily. Large doses of quinine are often useful in early cases of goitre, and dilute hydrofluoric acid (1 in 500), in doses of 20 to 60 minims, has been employed with success in its treatment. "*Soured milk*," prepared from a good strain of the Bulgarian bacillus, is a useful remedy, either alone or as an adjunct to other forms of medicinal treatment (Figs. 7 and 8).[1]

Autogenous *vaccines*, prepared from intestinal organisms belonging to the colon group, have been employed successfully in the treatment of recent cases of goitre (Figs. 9 and 10).[22], [23] These vaccines should be administered in increasing doses, varying from 150,000,000 to 1,000,000,000 of the organism, at intervals of one week.

An effective measure in the treatment of goitre consists in excluding the operation, or counteracting the effect, of those factors, which favour the action of the excitants of the disease by making undue demands upon the functional powers of the thyroid gland. The patient should, therefore, live under the best possible hygenic conditions of life in large well-ventilated rooms or in the open air, and at an altitude as near sea-level as possible; the dietary should be largely vegetarian, meat being restricted to once in the day. Constipation and intestinal disorders must be corrected, and the bowel freed of parasitic worms, if these should be present.

The patient must lead a life which does not excite the emotions, and, finally, in cases associated with the onset of puberty or of menstruation, and in those which persist *after* pregnancy, some preparation of *thyroid extract* should be administered. The liquor thyroidei (B.P.) is the most efficient of the preparations of the gland, but when this is not available, the fresh tabloids are very convenient and effective. Many cases of the disease, especially in young girls, respond readily to this treatment, combined with attention to the bowels; this is often all that is required to cause the disappearance of the swelling. Thyroid preparations act mainly by easing the strain on the hypertrophied gland. They are often ineffective where there is much intestinal fermentation, so that it is well, when employing them, to put the intestinal tract into as healthy a state as possible by the use of appropriate remedies. Indeed, if this is not done, the most efficient of thyroid preparations may be rendered devoid of beneficial action.

Thyroid extract is sometimes effective in cases which are not influenced by iodine. Its potency is increased by its combination with potassium iodide, or with arsenious acid in small doses. The initial dose (of thyroid gland preparations) should in all cases be small, and should be increased with

Plate XXIX.

Figs. 7 and 8.—*A case of goitre before and after treatment by "Soured Milk"; duration of treatment, 30 days.*

Figs. 9 and 10.—*A case of goitre before and after treatment by an autogenous oli vaccine. Number of inoculations, five; doses, 150 to 500 millions weekly.*

Fig. 11.—*Experimentally-produced cretinism in rat.* Age of all three animals 20 days. Note small size of the cretin animal and its scoliosis which is due to hypothyroidism.

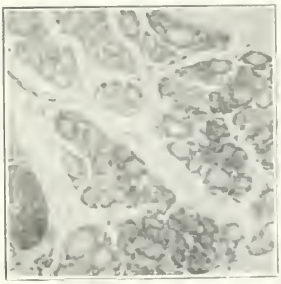

Fig. 12.—Normal thyroid gland of four-day rat.

Fig. 13.—Thyroid gland of four-day cretin rat. The parenchyma cells are almost entirely replaced by fibroblasts.

caution. The smallest dose which produces the desired effect is the dose to employ. When tabloid preparations are prescribed, care should be taken to ascertain their precise strength in terms of the fresh gland. Cardiac weakness is a contra-indication to their use.

One or other, or a combination of these measures will effect a cure in the majority of recent cases of parenchymatous goitre. Cases are occasionally met with, however, which, though apparently suitable for medicinal treatment, resist all measures which are employed; they are probably those in which a considerable degree of fibrotic change has occurred.

Congenital Manifestations of Endemic Goitre.—In addition to congenital goitre, which has been dealt with sufficiently, cretinism, cretinous idiocy, and deaf-mutism, are the common congenital manifestations of endemic goitre; these are to be found in all goitrous localities where the endemicity of the disease is high. They are developmental defects, dependent upon congenital inefficiency of the thyroid mechanism. This inefficiency may be complete or partial, and is due to the action of toxic substances present in the maternal blood on the developing fœtal gland.[24] It has been found that approximately 5 per cent. of the offspring of goitrous white rats, living under experimental conditions, are born with completely fibrosed thyroids (Figs. 11, 12, and 13), while no less than 63 per cent. show greater or lesser degrees of thyroidal or parathyroidal change at birth.[11] Endemic goitre does not give rise to cretinism or to myxœdema in the individual, though it may be responsible for some slight degree of hypothyroidism. Such manifestations of the effect of goitrigenous agents occur only in children of the second or third generation, and never in children as a consequence of the development of goitre in the individual.

The mothers of cretins are, in goitrous localities, almost always goitrous.[24] The goitres are usually of large size and the seat of secondary degenerative changes. The functional capacity of such goitrous thyroids, although it may be sufficient for the needs of the individual, fails in a small percentage of cases—approximately 5 per cent.—to respond to the increased demands of pregnancy; consequently, there is a sub-minimal deficiency of thyroid substance in the blood of such women.

The maternal thyroid is unable in such cases fully to counteract the action of the toxic substances present in the blood-stream, and these are free to exert their harmful effect upon the fœtal gland.[24]

There are certain factors which are of great importance in favouring the development of such a condition of thyroidal inadequacy in the goitrous pregnant woman. These are: (1) attacks of infectious diseases such as tuberculosis, erysipelas, acute rheumatism, rheumatoid arthritis, typhoid fever, influenza, intestinal disorders and helminthiasis; (2) psychic factors, such as fright, worry, mental depression, and impressions received by the mother during pregnancy.[24]

Endemic cretinism is commoner in the male than in the female sex. The proportion is as five of the former to two of the latter in my series of 203 cases.[24] It is much more common in localities where the endemicity of goitre is high, owing probably to the fact that the degree of degenerative change in the goitrous thyroid is often proportionate to the severity of the endemic. It shows a marked tendency to occur in certain families, a tendency which is also well illustrated by the occurrence of cretinism in the offspring of goitrous rats living under experimental conditions.[11]

About 50 per cent. of all cretins are goitrous. They are more liable to develop goitre than are healthy children, and their liability to it increases with increasing age.[24] The cretin comes into the world with a thyroid, which is either completely fibrosed, or which is in a state of partial fibrosis and hyperplasia that renders it extremely susceptible to the action of goitrigenous agencies. Those portions of the thyroid, which may have escaped complete destruction prior to birth, sooner or later succumb to the post-natal action of these agencies; the gland becomes goitrous, and rapidly undergoes adenomatous and other degenerative changes which may wholly deprive it of functional capacity. If, however, cretinoid infants are removed from the influence of goitrigenous agencies at as early an age as possible, the congenitally impaired thyroid may escape further destruction, and may serve in some measure to fulfil its function; the protection of such children from goitrigenous influences is, therefore, a curative measure of much value.

Fig. 14.—*Cretin aged [illegible] years in whom nervous symptoms were very pronounced.*

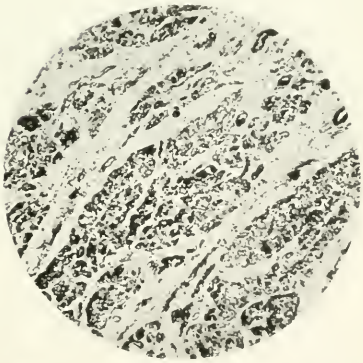

Fig. 15.—*Thyroid gland of cretin who exhibited pronounced nervous but very few myxœdematous symptoms; note the great increase of fibrous tissue and almost complete absence of colloid.*

PLATE XXXII.

Fig. 16.—*Goitre in fowl.*

As a rule, the presence or absence of a goitre—which is usually adenomatous—makes little or no difference to the well-being of the cretin. In rare cases, however, in which degenerative changes are probably not so pronounced, the development of a goitre may be of benefit to the cretin.[24]

Two types of cretinism are to be met with in endemic centres of the disease : (1) a myxœdematous type, which is that usually described in text books, and (2) a type in which mental and nervous symptoms predominate. The latter condition is one of cretinous idiocy with associated cerebral diplegia (Figs. 14 and 15, Plate XXXI.).[24] It appears probable that the peculiar type of cretinism is dependent upon the extent of the destructive lesion on the thyroid mechanism as a whole, and that involvement of the parathyroid glands may be responsible for some of the nervous symptoms from which these cretins suffer. It has been found that approximately 32 per cent. of the offspring of goitrous rats are born with congenital disease of the parathyroid gland,[11] while about one-third of all cretins exhibit the nervous symptoms referred to. The recognition of the fact that certain mental and nervous symptoms are in many cases the predominant evidences of congenital disease of the thyro-parathyroid mechanism is of great importance; for when treatment is commenced early enough such cases respond in the most remarkable way to thyroid medication.[25], [26].

A consideration of the ante-natal history, whether the mother shows obvious signs of goitre or not, may facilitate the early recognition of cases of congenital hypothyroidism. Especially is this the case with respect to the influence of acute infections on the mother during pregnancy, for the toxins of many acute infectious diseases have a profound influence, not only upon the maternal but also upon the fœtal thyroid mechanism, and may themselves be sufficient to impair or destroy this mechanism, whether their action be ante-natal or post-natal. Important as the whole question of ante-natal hygiene is, in no respect is it more so than in its bearing on the proper functional development of the thyro-parathyroid mechanism, the influence of which, as a regulator of metabolism and as an antitoxic agent, is so profound.

The various grades of cretinism, which are so readily recognisable, are the grosser evidences of congenital impair-

ment of this mechanism, but there are many lesser signs and symptoms of congenital hypothyroidism, which often escape recognition, and whose detection would be attended with results most beneficial to the backward children who are so afflicted. These, however, can rarely be detected till the end of lactation in breast-fed children; but from that time onwards such symptoms as slowness to walk or to talk, delayed and defective dentition, scoliosis, enuresis, or other signs of physical and mental backwardness should at least excite the suspicion that the underlying cause may be a congenital defect of the thyro-parathyroid mechanism.[31]

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EXOPHTHALMIC GOITRE.

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(With Plate XXXIII.)

It is proverbially ill to give a dog a bad name, but it is "miching mallecho"[1] to do the same by a disease. The dog you can always hang, but the disease, though it may not hang you, is liable to hang your patient, because its name has obscured its real character.

In the nomenclature of disease there are many instances of bad names, among the most conspicuous of which is that which heads this paper. The malady has been christened and rechristened and christened again. In this country it occasionally bears the name of Graves, the celebrated Dublin physician who described it in 1835. On the Continent it is usually called after Basedow, who redescribed it five years later. According to Sir William Osler, however, the credit really belongs to a physician of the City of Bath, Caleb Hillier Parry, who had called attention to it ten years before Graves. The name of the distinguished orismologist, who first called it exophthalmic goitre is unfortunately lost to fame.

In the later Victorian days, when reason pure and unimaginative was triumphantly but respectably ascendant, the practice of calling a disease after the person most prominently associated with it, came to be severely regarded. It was in consonance with pure reason that a disease should be called by a descriptive title, for what more reasonable than a name which proclaims an ætiology? Also, it was entirely in consonance with the proverbial generosity of scientists towards one another to ensure that no undue distinction should attach to him whose clearer vision had rescued an entity from the scrap heap of nescience. The pioneer is always a nuisance; he deranges pedagogic calm.

From this Pride's Purge of personalities in official nomen-

[1] Secret and insidious mi-chief (*Hamlet*, III., 2).

clature, Addison's disease was almost alone in escaping, and the simple dignity of "Graves's disease" became submerged under the pompous, pretentious and, as it now turns out, almost wholly irrelevant cacology of "exophthalmic goitre."

Altogether irrelevant the name is not, for it fixes upon the two superficially most salient features in a typical case. Inasmuch, however, as the disease may, and often does, exist without either ocular prominence or thyroid enlargement, the title cannot be said to suggest the ætiology, which is, in truth, still a great mystery. To attain to a solution we must divest our minds of such shallownesses as exophthalmos and goitre, and turn our attention to deeper things.

The latter-day endeavours in this direction have been laudable, but unfortunate. In our desire to simplify the complexities of internal secretory problems, we have taken each individual endocrinic gland and have indicted it either with the brutality of excess or the cowardice of insufficiency. Just as the older oculists acknowledged myopia and hypermetropia, but could not realise astigmatism, so seemingly are we unable to imagine the existence of a disturbance which is neither a pure excess nor a pure inadequacy. Thus it has come about that Graves's disease is now in serious danger of suffering yet another christening, more misleading than any of the others, a sort of adult total immersion from which it shall issue forth, freed from former terminological heresies and clad in the simple, unsullied garment of "hyperthyroidism."

Against this threatening catastrophe I desire to enter a protest. Whatever it may be, or may not be, Graves's disease is not a pure hyperthyroidism. I have never seen a case, and I do not believe that there has ever been one, which to careful observation did not reveal the existence of some symptom or symptoms which proclaimed the presence of thyroid insufficiency side by side with those of the obvious thyroid excess. Moreover, real hyperthyroidism, a hyperthyroidism, that is, which has been artificially induced, does not succeed in evoking the picture of exophthalmic goitre. So far as I am aware it has never been claimed that thyroid enlargement has thus been effected; and although cases are on record in which ocular protrusion has been provoked in

this way, such cases are extremely rare. It is indeed no longer possible to speak of proptosis as the result of hyperthyroidism, for Maurice[1] of Lyons has shown that this symptom denotes an excessive action, not of the thyroid, but of the suprarenals. Little, then, as I love "exophthalmic goitre," I dislike "hyperthyroidism" more.

There is a condition which is more common than is usually supposed to be the case, in which a simple parenchymatous goitre suddenly lights up and produces the complete clinical picture of Graves's disease. In France they speak of this as "un goitre basedowifié." That a beautiful language like the French language should tolerate such an abdominable monstrosity as "basedowifié" shews the necessity for some such verbal adjective. I suggest that in English the word "begravesed" would be convenient and not uneuphonious. Here, if any were wanted, is an additional reason, while forsaking all others, for retaining, as the title of this disease, the name of the distinguished Dublin physician who courageously fed fevers.

I have already ventured in the pages of THE PRACTITIONER[2] to express a doubt as to the thyroid gland being the original offender in the causation of the disease. Further experience has much intensified that doubt. The case which has most impressed me is that of a doctor's wife, whose symptoms were diagnosed about ten years ago by a very eminent and skilful physician as Graves's disease, without either exophthalmos or goitre. Another physician, scarcely less eminent, advised the removal of the atrophied rather than goitrous gland, whose perverted secretion he believed to be the cause of the ever-increasing symptoms. The thyroid was accordingly removed with all the thoroughness which characterises the work of the surgeon selected for the operation. It is now eight years since the operation was performed, and when I first saw the patient a few months ago she presented a typical instance of those curious cases, which are more numerous than is generally supposed, in which the symptoms of myxœdema co-exist with those of Graves's disease. An interesting feature in the case was the

[1] *Lyon Medical*, October 20, 1912.

[2] "The Therapeutic Promise of the Internal Secretions," November, 1911.

inability of the patient to tolerate thyroid extract even in minute doses. An endeavour to overcome this difficulty had been made by several operations for grafting, the results of which, though more or less successful, proved unfortunately to be transient. Some success was ultimately attained by associating a thyroid with a parathyroid preparation. The addition of the latter promptly relieved some of the symptoms, especially the intolerable sense of chilliness from which the patient had hitherto suffered.

Parenthetically, let me say that I have known two cases of paralysis agitans which had originally been diagnosed as Graves's disease. The mistake in both instances arose from the association of tremors, mental restlessness, tachycardia, intolerance of heat and some degree of ocular prominence. The beneficial effect of parathyroid extract in paralysis agitans is well known.

But, it may be asked, if the thyroid gland is not the real villain in the tragedy of Graves's disease, where is that villain to be sought? This is a riddle which has still to be unravelled.

It has frequently been pointed out that the enormous preponderance of females over males in the sex-incidence of the disease ought to afford some clue to the mystery, a clue which seems to attain an added importance from the fact that the uterus of the pœlœstrachian ancestor is developed from the thyroid gland. Talleyrand described man as "une intelligence contrariée par des organes." With characteristic caution he refrained from defining woman in similar terms; but it is obvious that a true estimate would give not only prominence, but predominance to the sexual organs as the disturbing factors in her case. And such disturbances are, most of them, reflected in the thyroid, which, as is well known, enlarges at puberty, during menstruation, during sexual excitement, and during pregnancy. Moreover, Graves's disease is generally preceded and always accompanied by menstrual difficulties. It is practically confined to the period of woman's reproductive activity. The thymus gland normally disappears on complete development of the sexual organs. In Graves's disease the thymus is, as the French term it, in reviviscence.

And yet, in spite of all this, clinical experience lends no support whatever to the suggestion that the real villain has

his abode in the uterus or its appendages. We must look elsewhere.

I have often noticed that the eyes of the victims of Graves's disease are set at what is called the celestial angle. The fissures run from within outwards and upwards, like the Chinaman's, instead of outwards and downwards as is normal in the Caucasian races. I used at one time to regard this, as I still regard both Stellwag's sign and von Graefe's, as an effect inevitable of the ocular protrusion. More careful observation has, however, convinced me that such is not the case. All the victims do not present this phenomenon, but a very large number do; and so impressed have I become with its frequency in Graves's disease that I have come to regard people, especially girls, who have eyes at the celestial angle, as candidates for the disease in its full efflorescence. The phenomenon is already recognised in medicine as one of the outstanding stigmata of idiocy of the Mongolian type, and it is not unreasonable to suppose that there may be some connection between the two maladies. Mongolism is a congenital condition.[1] Graves's disease is essentially a post-natal condition. Garrod has recorded some cases which occurred in childhood and even in infancy, but the manifestations are generally delayed until puberty or thereafter.

About the pathology of mongolism nothing appears to be known. It is evidently not due to any gross lesion, for autopsies leave us unenlightened. That it is due to developmental failure somewhere is quite obvious, and the evidence points very strongly to the endocrinic system as the seat of that failure. The disease is superficially related to cretinism, from which, however, it is quite distinct. In the autopsies of cases of mongolism, the thyroid is almost always reported as normal, but I cannot find that in these cases a systematic search has been made for evidence of lesions in the other internal secretory glands. The interest in the matter is probably still too recent to admit of the accumulation of sufficient material.

Garrod has called attention to the association of congenital

[1] The serio-comic story of the French father deserves to be re-told here. On being shown the baby, a Mongol, by the monthly nurse, his horror-stricken exclamation was "Grand Dieu, elle m'a trompé; c'est un petit chinois!"

morbus cordis with mongolism. Trousseau, in 1872, showed that people with aortic disease were peculiarly liable to Graves's disease, and Lepine, in 1906, made the same observation with regard to mitral disease. In typical Graves's disease cardiac disturbance is one of the most serious features of the condition. The other is mental disturbance.

The importance of mental disturbance in Graves's disease is not always estimated at its true value. It is a matter for most anxious consideration in every case. The disturbance may proceed to the point where certification is necessary, and even in the most favourable circumstances it completely changes the character and disposition of the victim. And this change is permanent. For although the obvious physical signs may improve or even disappear, the mentality remains disturbed until the end.

Now it is interesting to note that the type of disturbance is not altogether dissimilar from that which occurs in mongolism, especially when we take into consideration the difference in the ages of the patients who come before us. The majority of mongols die in childhood; the majority of those suffering from Graves's disease begin their troubles after puberty. Writing of mongols, Shuttleworth says: "These children are very imitative, are fond of music and dancing, and see the comic side of everything." There is scarcely a subject of Graves's disease who does not exhibit the artistic temperament in the full effulgence of its irresponsible egotism.

In spite of some conspicuous exceptions which are in my mind, I would go so far as to say that by far the greater number of the subjects of Graves's disease are degenerates. The victim, like the poet, is born, not made. The machine is initially so badly balanced that puberty, a slight shock, an emotional disturbance, so seriously upsets it that it can never be completely restored.

I venture to suggest that Graves's disease may bear the same relationship to mongolism that myxœdema bears to cretinism. The one is the delayed, adult and incomplete manifestation of an intra-uterine fault of which the other is an immediate and complete example. That the subject of Graves's disease bears no very striking resemblance to the mongol may be explained by the analogous dissimilarity between giantism

and acromegaly, both of which are due to the same underlying excess of pituitary activity. Giantism displays the result of that excess in the sapling; acromegaly, in the mature tree.

The peculiarity in the development of the bones forming the orbit which is characteristic of mongolism and noticeable in Graves's disease, suggests that in the defect which underlies these two diseases the pituitary may play an important part.

In favour of the complicity of the adrenals there are several suggestive facts. One has already been mentioned, namely the responsibility of these glands for the production of proptosis. Another is the facial expression of "fright and flight" presented by the patient, the association of which with supra-renal activity has been so well shewn by EHiott. Another which is not without significance is that so reliable a physician as the late Dr. Gibson, of Edinburgh, was a strong advocate for the treatment of the disease by supra-renal extract. Finally, pigmentation of the skin, which is rarely absent from complete Graves's disease, and the nature of that pigmentation, suggests some association with the cause of Addison's disease.

So much then for the nomenclature and ætiology. Concerning the symptoms and diagnosis of this readily recognisable disease, there is little to say which is not already familiar to readers of THE PRACTITIONER. Peter put the physical signs in a nutshell with the phrase "un gros cœur, un gros cou, de gros yeux." If he had added "tremors of the hands and of the brain" the picture would have been substantially complete. Under "gros cœur" must of course be included the heart-hurry without which, as Hector Mackenzie properly insists, it is impossible to make the diagnosis. It is not only a constant symptom, but is usually one of the earliest to appear, and among the last to disappear. What I have just referred to as "tremors of the brain" are the mental symptoms. These vary considerably both in degree and in kind, but a sense of restlessness, both physical and mental, is characteristic and constant even in early and slight cases. But that is not all. Whatever she may previously have been, the patient now becomes irritable, assertive and wilful, unreasonable, wrong-headed and "difficile"

to the last degree of impossibility. To make matters worse the intelligence is not only unimpaired, but it is often hyperacute. The fondness for music, the drama, for artists, actors, and tenors is a pronounced and often a pathetic feature. There is usually disturbance of the sex instinct, which not infrequently takes the form of perversion. The mental element has been much less conspicuous in—it may indeed be said to have been absent from—the few cases of the disease which I have seen in men. The female of the species is evidently more deadly than the male.

The prognosis as to life is not very difficult to estimate in an individual case. When the vascular disturbance is considerable and the emaciation rapid I augur ill of the disease. Gastro-intestinal complications, such as diarrhœa and vomiting, are generally of very evil omen. When the disease makes its first appearance about the time of the menopause, the outlook is not favourable. In this, as in many other respects, it is the dangerous age. Otherwise, the prospects of something approaching to complete recovery are by no means bad. It is, however, very doubtful whether, in pronounced cases, recovery is ever really complete. It is said that relapses are common; the real truth in such cases is probably that the so-called relapse represents the flaring-up of symptoms which had merely been sleeping under the thin ashes of a seeming peace.

But whatever may be the truth in connection with the physical signs I am quite convinced that in a marked case there is never on the mental side a complete *restitutio ad integrum*. It is recognised that a person who has once been an alcoholic or a morphinist, though he may completely relinquish the baneful habit, never quite regains his lost standards. He remains unreliable and as often as not he is a gaudy, gratuitous and unconvincing liar. The poison has for ever removed the delicate bloom from his character. With Graves's disease it is much the same. Not that the sufferer displays the same faults of character as the alcoholic or the morphinist, but the alteration wrought by the disease persists and even deepens, though all else may seem to recover. By this I do not mean the restlessness which often seems to wear itself out. I refer to the change from docile to aggressive,

from reasonable to impossible, from neighbourly to selfish, which, once effected, always remains.

I have often been asked whether a girl who has, or who recently has had, Graves's disease, ought to marry. The answer to such a question depends upon the view which one takes as to what should constitute a bar to marriage. In spite of the unsightly exorbitism, on account of their mental sprightliness and their artistic tastes, these girls are often quite attractive. Their parents and brothers will nevertheless tell you that, like David Hume, they are "gae ill to live wi'." "There is no one," sang the Psalmist, "but lusteth to live good days," but the man who takes unto himself a begravesed spouse may bid farewell to his chances. His days will be filled with apprehension, and his nights with dismay. I have known one such, and he was a very busy man, who had to walk three miles in the middle of a stormy winter's night to buy a thermometer, because she thought she was going to be feverish. It is probable that in the eugenic Utopia such women will not be allowed to marry, for not only do their vagaries impair their husbands' social efficiency, but it is very doubtful whether they are capable of bearing altogether satisfactory children. My experience is too small to permit me to dogmatize, but most of the children of begravesed mothers whom I have seen, have been degenerates. I cannot recall a single one who in every respect was perfectly normal, and I have seen a very large number who were the reverse.

The treatment of Graves's disease is symptomatic, and must so remain either until clearer ætiology lights us to a better way, or clinical methods are more successful than they are at present. Owing to the menace of the circulatory disturbance, the primary indication is rest. Lest the heart bend under the influence of the unseen goad, its ordinary work must be reduced to a minimum. In severe cases, therefore, bed is the only place for such a patient. When asked for how long this discipline is to last the cautious physician will hedge. For a discipline it is, and one to which, on account of the restlessness which afflicts the patient, it is very difficult for her to submit. Many there be who, after a few days, break into open rebellion, roundly declare the doctor to be an ignoramus, and arise to resume their activities of meddle and muddle with all the

energy and truculence of which they are so capable. I once told such a lady that the only way in which she could find salvation was by breaking her leg. In a fortnight she had done so. This was three years ago, and her husband tells me that she still considers that I was the cause of her accident. This is typical of the psychology of the disease.

If the all-essential rest can be obtained in the country or at the seaside in a sedative climate on open-air principles, much better results are secured than when "rest" connotes a system of stuffing a sensitive stomach in a noisy nursing home in a mean and malodorous street. When this system includes electricity, massage and isolation, the conditions conducive to dismal failure are fairly complete. But though isolation, as usually understood, is both senseless and futile in these cases, it is nevertheless a great advantage to remove the patient from her ordinary surroundings to an atmosphere of restraint and routine and discipline. I have known cases, but they have been few, in which considerable benefit was obtained by suggestion. From hydrotherapy at ordinary spas I have never seen good results; but I have known many patients to derive conspicuous and lasting benefit from a course of treatment at Divonne, where the physicians have made a special study of the disease, and where they treat the patient rather than the complaint.

To treat the patient and not the disease is, of course, one of the therapeutic aphorisms which we serve in speech and neglect in practice, but he who neglects it in the presence of Graves's disease will fail where he might succeed. An enormous number of drugs have been recommended as useful by an enormous number of more or less competent clinicians. Some of these drugs are useful in certain stages, and where certain symptoms predominate; but many of them are useless, and some are altogether and utterly bad. Among the last-named the classical sedatives and hypnotics take the first place. On the face of things it is easy to suppose that restless, breathless, sleepless busybodies, as these patients always are, would benefit by the bromides of the alkalies and their latter-day congeners, such as sulphonal and veronal. But they do not; or if they do so temporarily, the immediate advantage is purchased at the price of subsequent long-con-

tinued disadvantage, by no means least amongst which is the almost insuperable difficulty of weaning the patient from the drug. The only bromide which is of use—and it is often useful beyond expectation—is the bromide of quinine. If, however, it does not succeed in producing evident amelioration in a fortnight, it should be discontinued.

Of latter-day drugs, the only one with any claim to be called a sedative which is at all admissible is aspirin, and that has occasionally seemed to me to be of undoubted value, quite apart from such sedative effects as it may possess. An exception may also be made in favour of belladonna in so far as that drug can be described as a sedative. Its value, however, which is not infrequently considerable, is due less to its sedative influence than to its controlling power over the perverted and superabundant secretion of the peccant gland.

One of the many functions of the thyroid is concerned with the metabolism of the calcium salts, and I have often thought that patients have shown very definite improvement after taking chloride of calcium (10 grs. ter die). The salt seems to give the thyroid some definite and useful work to do, and thus in some degree to preserve the patient from the effects of its furious raging.

It is entirely in accordance with the spirit of the age that the surgeon should have come to regard the goitre of Graves's disease as a suitable field for his activities. He asserts that medical treatment is a failure; that surgical treatment is substantially free from risk, and produces brilliant results. When confronted with statistics to show that satisfactory and lasting benefits are obtained by the physician, he replies airily that "it is very doubtful whether all these cases were true examples of Graves's disease." No such reservation is necessary in the case of the statistics adduced on the surgical side, for it is not possible that a surgeon's diagnosis of medical disease could ever be at fault. And what are the advantages which the patients are to derive from these surgical deeds of derring-do? For an answer let us hearken unto the words of one of their latest and most persuasive advocates. "Usually within a month or six weeks of operation, the patients are able to get about in comfort, but exertion is followed by an increase in the pulse, and by a certain amount of dyspnœa. The

PLATE XXXIII.

Fig. V.

exophthalmos is more slowly recovered from, and although this may be considerably decreased, even within a fortnight of the operation, the eyes at once become prominent when the patient is excited."[1] Here, indeed, are results so truly marvellous as to justify almost any risks. The operation is successful, but thereafter exertion is unfortunately attended with tachycardia and dyspnœa, and the slowly receding exophthalmos is rude enough to reappear as soon as the patient is excited. Verily, the mere physician must hide his head in the presence of such brilliancy.

And are they permanent, these staggering successes? It would seem not. Here (Fig. A) is a portrait of a young woman, the scar of whose operation is quite visible in the picture, on whom an operation was performed about three years before the photograph was taken. She had risked much, but she does not appear to have gained much. A more perfect example of the classical features of the disease it would be difficult to find. And she is not a single spy; scattered over Europe there must be battalions of them.

The truth is, these operative procedures in Graves's disease represent the heroic application of loose conclusions from insufficient data. In spite of all that it is possible to urge in their favour, it must be obvious to any thinking person that, so far as their immediate consequences are concerned, these operations are by no means free from serious danger. From the above quotation it is equally obvious that the best obtainable results are but "*dérisoires*" and do not in any case exceed those which may be confidently expected of careful medical treatment. Where, then, is the excuse for operative measures?

If it could be established that the real seat of the disease was in the thyroid, it would be possible on theoretical grounds to justify interference with this gland. But so far from such a proposition being established, the evidence points strongly, even overwhelmingly, in the direction of showing that the thyroid is merely an unwilling agent in the production of the symptoms, and reflects, reluctantly enough, a disturbance which originates elsewhere. An almost analogous case may be found in the behaviour of the kidneys in diabetes. Their secretion is not only largely increased, but it is perverted; it contains sugar which it ought not to contain. It would be as reasonable,

[1] The Practitioner. October, 1914.

as scientific, and as effectual, to remove one kidney for glycosuria, as it is to ablate one lobe of the thyroid gland for the relief of Graves's disease.

Most of those who are interested in the matter of the treatment of Graves's disease have searched patiently for some endocrinic remedy. By a curious, and to my mind wholly illogical conception, it was thought that the blood or serum of an animal from whom the thyroid gland had been removed would, when administered to a begravesed patient, succeed in evoking order out of chaos. Antithyroidin (Moebius), hémato-éthyroidine (Carrion and Hallion) and thyroidectin have all been introduced in accordance with this conception. I have tried them all, and with the exception of Carrion and Hallion's preparation, which seemed to do good in one case, I have found them quite inert, as, indeed, I fully expected to do. Harrower, in his excellent manual on *Hormone Therapy*, says: "Beebe has evolved a valuable method of treating hyperthyroidism by means of an antiserum produced by inoculating a thyroid preparation into rabbits and sheep. Further information regarding the details of this treatment may be found in his book.[1] Its value has been demonstrated in more than three thousand cases, and a number of very good results have been obtained." I have not yet had an opportunity of trying this preparation.

Diligent endeavours have been made by many observers to find the clue to the treatment of Graves's disease in some endocrinic gland other than the thyroid. Gibson, of Edinburgh, thought he had succeeded in inculpating the adrenals, but none of us have, unfortunately, succeeded in confirming the observations of this careful and conscientious physician. I have myself on circumstantial evidence indicted the ovary, the pituitary, the parathyroid, the thymus, and even the liver, with no better result than a sorry and sorrowful verdict of "not proven." Ever and anon what seemed at the time to be striking successes have lured me into the belief that I had read the whole riddle. Then, with some disheartening failures would come disillusion, and the question has been regretfully but firmly returned to the crucible. That is where it rests at present. And that is where, for the moment at any rate, I must be content to leave it.

[1] *The Diseases of the Ductless Gland.*

THE PARATHYROID GLANDS.

By ARTHUR F. HERTZ, M.A., M.D., F.R.C.P.

Physician to, and Physician in charge of the Neurological Department Guy's Hospital.

THE anatomy of the parathyroid glands was first accurately described in 1880 by Sandström,[1] who regarded them as embryonic rests of thyroid tissue. Various observers had noticed them before, and had described them as small lymphatic glands or accessory thyroids. Between 1891 and 1897 Gley[2] published the first experimental observations on the physiology of the glands, from which he concluded that the tetany which may follow operations on the thyroid glands is due to injury or removal of the parathyroids.

In spite of a considerable amount of anatomical, physiological, pathological and clinical work on the subject, very little real advance has been made in our knowledge of the parathyroid glands in the last 15 years, and it is very difficult to draw any definite conclusions from the mass of contradictory literature which has been published.

There are generally four parathyroid glands; Forsyth has shown that they occupy the same compartment of the deep cervical fascia as the thyroid gland, with which they are generally in contact and in which they may actually be buried. Most commonly they are situated along the posterior borders of the gland near the entry of the inferior thyroid arteries.

The observations of MacCallum[3] appeared to show that the parathyroid secretion controls in some way the distribution of calcium in the body. When the secretion is deficient, the tissues lose some of their calcium. As calcium moderates the activity of nerve cells, this results in an exaggeration of nervous excitability, which generally manifests itself in tetany. Consequently the administration of parathyroid glands or of calcium salts has been found, both in animals and in man, to be equally efficacious in controlling tetany due to injury or removal of the parathyroid glands. But the disturbances

in calcium metabolism, upon which tetany appears to depend, may occur when the parathyroid glands are normal, as in the tetany of rickety children, and that which is associated with dilatation of the stomach and pregnancy. In such cases the administration of calcium salts is sometimes of value, but that of parathyroid gland is useless. It is possible, however, that the secretion of the parathyroid glands is sometimes deficient in these conditions and so helps in the development of the tetany, although there may be no definite structural abnormality in the glands.

In opposition to the views of Gley, MacCallum and most other investigators, Forsyth [4] concluded, from a very thorough investigation of the anatomy of the parathyroid glands, that it is almost impossible to excise them completely without seriously injuring the thyroid gland. On this account, and from the fact that a considerable percentage of animals from which Gley believed he had removed the glands suffered little or no ill results from the operation, Forsyth believes that the parathyroids have no connection with tetany. In his opinion they are portions of the main thyroid gland, which have no separate function but secrete the same colloid substance as the thyroid gland, though they have not yet formed vesicles; they may, however, develop into thyroid tissue, for intermediate types occur.

It has been suggested that paralysis agitans is due to disease of the parathyroid glands, but no pathological changes have been observed after death, and in a series of about a dozen cases Dr. W. Johnson and I found that a preparation of parathyroid glands taken by mouth had no effect on the symptoms or course of the disease.

I have only seen one case in which symptoms appeared to be due to parathyroid insufficiency. The result of treatment with parathyroid gland was so striking that it is difficult to believe that the symptoms could have been produced in any other way. I have not been able to find a record of any similar case.

CASE OF PARATHYROID INSUFFICIENCY CURED BY THE ADMINISTRATION OF PARATHYROID GLAND.[5]

The patient, C. H. G., a clerk, aged 47, first noticed an

enlargement of his thyroid gland when he was 30. It gradually became very large, and in 1908 the greater part of it was removed. After this, he remained perfectly well until August, 1910, when he was in very good health and weighed 191 lbs. He then quite suddenly became extremely depressed, very nervous and restless. He had an irresistible desire to keep moving and slept very little, walking about the greater part of the night. He was exceedingly tremulous, so that he found it difficult to write; there was a continuous fibrillary twitching of the eyelids, but there was no tetany. His general appearance was similar to that of a severe case of Graves's disease, except that his eyes were sunken instead of being prominent, and no thyroid gland could be felt.

Though his appetite increased, and he ate enormously and was never sick, he lost weight rapidly, so that he was only 144 lbs. when I first saw him with Sir Bertrand Dawson on the 2nd of December 1910. He experienced some difficulty in swallowing, the food appearing to stick in his throat; and he also had some irregular intestinal pains. The X-rays showed that the dysphagia was due to irregular spasmodic contractions of the œsophagus, and perhaps a similar condition accounted for the intestinal pain.

His pulse was constantly about 120, and he was greatly troubled with palpitation; his face and neck were deeply flushed. His hair had ceased to grow, but it did not become thinner. Formerly it required to be cut every ten days, but now six weeks had elapsed without any increase in length occurring, this was also noticeable to a less extent on his face. He had become completely impotent. Instead of opening his bowels once a day as before, he now passed three or four large, but otherwise normal, stools each day. His urine was scanty, but otherwise normal. The secretion of sweat was unaffected.

We thought that the condition was due to disturbance in the secretion of some of the ductless glands, possibly as a result of the operation, which might have injured the parathyroid glands at the same time as the greater part of the thyroid was removed.

On being put to bed and given four pints of milk a day, in addition to an ordinary full diet, his pulse became slower

and his abdominal discomfort disappeared. His weight continued to fall, till it reached 130½ lbs. on December 13th, and he found it excessively difficult to stay in bed on account of his restlessness. Dry thyroid gland aggravated the symptoms, and Moebius's antithyroid serum made him sick. He was given large doses of opium and bromide, which had the effect of making him slowly gain weight till he was 159 lbs. on February 6th, 1911; though the pulse was slower and the restlessness and tremor less marked, his other symptoms were unaltered.

He was allowed to get up in February and return to work. His weight at once began to fall, though slowly, and in spite of continuing with the same diet and taking opium and bromide, he only weighed 127½ lbs. on June 18th. He continued his work, but on that day began to take $\frac{1}{10}$ gr. of dried ox parathyroid gland (Armour) four times daily, and four days later he discontinued the opium and bromide. He gained 6½ lbs. in the first four days, 12 lbs. the next five days, 5 lbs. the next four days, and 5 lbs. the next six days, making 28½ lbs. in nineteen days. At the same time he became stronger every day, slept better, was less restless, the tremor and dysphagia disappeared, his hair began to grow, the quantity of urine increased, the stools diminished in bulk, and the pulse fell till it became slower than normal.

In a month he was almost well, but it was not until he had been taking parathyroid gland for six months, that his sexual functions returned. By January 11th, 1912, he weighed 161 lbs., and at Christmas, 1912, he weighed 175 lbs. He then discontinued taking the parathyroid preparation. Though by August 1913, he had gained another 4 lbs., he was more restless and his pulse was faster than it was in 1912; he was therefore advised to continue to take $\frac{1}{10}$ gr. of dried parathyroid gland daily, which he continued to do until November, 1913, when he discontinued it, as his face had assumed a brick-red colour, his throat was somewhat full, and the vessels in his neck throbbed. These symptoms disappeared after omitting the parathyroid.

His weight in February 1914 had risen to 189 lbs.; he

felt perfectly well and strong and no trace of nervousness remained, although he was working very hard.

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THE PHYSIOLOGY OF THE CHROMAFFIN SYSTEM.

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THE history of the elucidation of the function of the chromaffin tissue affords one of the many examples of the way in which the observations of the clinician have led to important physiological discoveries.

Schäfer has told how Dr. Oliver observed that the administration of an extract of supra-renal gland to his son caused sickness and constriction of the radial artery, and how he brought the preparation to Schäfer and asked him to test it on an animal. The extraordinary rise of arterial pressure produced showed that the extract contained some substance of great physiological activity, and led Oliver and Schäfer, and subsequently many other physiologists, to undertake the extensive series of investigations by which our present very complete knowledge of the functions of the medulla supra-renalis, or to speak more generally, of the chromaffin tissue, has been gained.

To-day the consideration of the chromaffin tissue may be separated quite definitely from the consideration of the cortex supra-renalis. Five years ago no writer would have dreamt of dissociating the medulla from the cortex of the bodies, and even at the present time there are some who may doubt the propriety of so doing. But there can be no doubt that, in the light of our knowledge of the distribution, development, and physiology of these structures, we are not merely warranted, but are compelled to make the distinction. While this is so, the intimate association of the two structures in man renders it impossible to deal with the one without some reference to the other.

The chromaffin tissue may be defined as a tissue composed of cells derived from the nerve cells of the abdomino-thoracic sympathetic system, which stain a brown colour with chrome salts, and produce a physiologically active substance called adrenalin.

Very early in embryonic life, before the neural folds have closed in to form the spinal cord, an emigration of neuroblast cells begins. Some of the cells which thus wander out, come to rest as a series of clumps just in front of the spinal cord, one clump on each side between each pair of vertebræ. These constitute the *ganglia of the sympathetic chain*. Other cells wander further afield; some of them come to rest in various clumps scattered throughout the viscera, and become the *visceral ganglia;* while others become scattered and spread out as a network in the walls of various hollow organs to constitute the *terminal ganglia*.

Certain of the cells which come to rest in the vicinity of the cord, instead of throwing out processes and becoming nerve cells, manufacture the material which stains brown with chrome salts; this is the internal secretion of the chromaffin tissue—adrenalin, or its immediate precursor.

The emigrated cells, whether nerve or chromaffin, do not lose their connection with the central nervous system. From cells remaining in the cord, processes extend outwards as nerve fibres, and end by forming branching dendritic processes round the emigrated cells. The fibres which pass from the central nervous system to the cells in the ganglia are the preganglionic fibres—the fibres extending from these are post-ganglionic. Some of these preganglionic fibres terminate in close association with the cells of the chromaffin tissue, and, as will afterwards be shown, act directly upon them.

The cells of chromaffin tissue are thus essentially the same as the cells of the abdomino-thoracic or true sympathetic system.

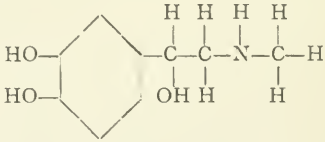
While in mammals they are massed chiefly in the medullary part of the supra-renals, they are also found in clumps or ganglia outside of these organs. In some animals, such as the rat, these supplementary masses are very abundant. In man, they are found at the branching of the carotids and at the branching of the aorta. In fish, the chromaffin tissue lies quite apart from the representative of the cortex supra-renalis—the *inter-renal* bodies. It constitutes a separate *adrenal* body or bodies.

The intimate association of the cortex and medulla supra-renalis in mammals has rendered it impossible to investigate

the effects of removal of either. Biedl has taken advantage of their separation in fish to excise the inter-renal bodies, and he finds that the animals become weak and slowly die. Whether removal of all the chromaffin tissue is compatible with the maintenance of life has not been decided. According to the observations of Elliot, the most prominent symptom in the cat, deprived of both its supra-renals, is a very marked fall of blood pressure. But it must be remembered that removal of the supra-renals leads to great debility, and that death supervening on debility from any cause is preceded by a very marked fall of arterial pressure.

Removal of the supra-renals having thrown so little light upon the physiological significance of the chromaffin tissue of the body, we have to turn to a study of the action of extracts of the tissue.

Oliver and Schäfer, and Swale Vincent, have found that the active product is formed in the medullary part of the gland. More recently, Takamine succeeded in isolating the active principle—ortho-dioxy-phenyl-ethanol-methylamine, which he called adrenalin.



That this is not a product of post-mortem change in proteins, as is the β-imidazolylæthylamin isolated by Barger and Walpole from putrid meat, is shown by the facts that it may be prepared from the gland during life, and that its amount in the blood of the supra-renal vein may be increased by stimulation of the nerves going to the glands.

The adrenalin formed by the chromaffin tissues, along with the iodothyreoglobulin produced in the thyroid, are the only definite internal secretions which have as yet been isolated. Adrenalin is essentially a stimulator or activator, hence the term hormone may properly be applied to it. But, unfortunately, this term has come to be applied to all internal secretions, whether they excite or depress, so that its use is apt to be misleading.

Adrenalin has not only been isolated from the medulla supra-renalis, but it, and some of its congeners, have been prepared synthetically.

Its presence is readily recognized not only by the physiological tests which will later be referred to, but by various chemical reactions depending upon the ease with which it is oxidized. A solution of adrenalin upon standing exposed to air rapidly takes on a red colour, and loses its activity. The change may be hastened by the addition of chlorine water.

The most delicate chemical test yet devised is that of Folin, Cannon, and Denis. It depends on the fact that adrenalin strikes a blue colour with phosphotungstic and phosphoric acids and sodium carbonate; and that the depth of the colour may be compared with that of a standard colour struck by the same reagents with uric acid. By this method as little as 1 in 3,000,000 of adrenalin may be detected. The quantitative accuracy of the test has been proved by comparison with physiological tests.

Adrenalin is a specific product of chromaffin cells, and these are essentially cells of the abdomino-thoracic or true sympathetic. When injected into the blood-vessels, it stimulates the terminations of these particular fibres in visceral muscle and in glands, and it acts on these terminations alone.

Its most striking and manifest action is upon the vascular system. Stimulation of the true sympathetic fibres generally causes constriction of the arterioles and augmentation of the heart. These conditions are produced by the intravenous injection of even very small doses of adrenalin—as little as 0·005 mg. per kilo of body weight, in a dog or cat, being sufficient to raise the arterial blood pressure. But, while stimulation of the abdomino-thoracic nerve causes constriction of most of the arterioles, the result is by no means uniform throughout the vascular system. It is most marked in the abdominal vessels; it is hardly manifest on the vessels of the lungs and cranial cavity. In the coronary arteries in the wall of the heart an actual dilatation is produced. And so it is with adrenalin. Its action is most marked on the abdominal vessels, only slightly manifest in the pulmonary and intracranial vessels, while in the coronary arterioles it causes a dilatation.

This marked action on the abdominal vessels may lead to an increased flow of blood to the limbs, and to an actual increase in their volume; it always leads to a congestion of the vessels of the lungs and of the cranial cavity.

This action on the vessels is most readily produced by intravenous injection. To produce it by hypodermic injection, very large doses are necessary. Intra-muscular injection may cause it fairly readily, apparently because blood-vessels have been lacerated. It is a question of rate of absorption, and since this varies so much, the use of adrenalin by subcutaneous and intra-muscular injection is uncertain, and may even be dangerous. Administered by the mouth, it has no general effect.

But, while the doses usually injected in physiological experiments cause constriction of arterioles and a rise of arterial pressure, Hoskins and McClure have shown that very small doses cause a dilatation and a fall of pressure. Desbouis and Langlois have found that, in the pulmonary vessels, large doses cause constriction and small doses dilatation.

Oliver and Schäfer showed, by perfusing the limb of an animal separated from the central nervous system, that the action on the arterioles is a peripheral one. The question of how it acts on these vessels has to be considered. Does it act upon the muscle fibres or upon the terminations of the nerves in them?

In answering this question, pharmacological methods have proved of use. Dixon found that adrenalin no longer acts after large doses of apocodeine, while barium still constricts the arterioles. The conclusion seems to be that barium must act upon something peripheral to that upon which apocodeine and adrenalin act—namely upon the muscle fibre, and that the two former must therefore act upon something either in the nerve or between the nerve and the muscle. On the other hand, Cathcart and Clark find that nicotine decreases or abolishes the action of barium, but does not decrease or abolish that of adrenalin.

It must be confessed that nothing is more difficult than to draw satisfactory conclusions from the antagonistic action of drugs. As Magnus so well points out, the element of

dosage is of much importance, the action of large doses being often the reverse of that of small doses. Again, antagonism in one locality does not imply a universal antagonism. Thus, Cushney has shown that atropine prevents the action of pilocarpine on the uterus, but has no effect on the result of stimulation of the hypogastric nerves, or on the action of adrenalin. In other situations, such as the salivary glands, it blocks these actions.

In considering the exact seat of action of adrenalin, physiologists have perhaps too much ignored the terminal ganglia which, in the case of the intestine at least, have such important functions. These ganglia are certainly present in many other situations. The investigations of Pollock upon the iris tend to show that the terminal ganglia persist after section of the nerves to the structure. The so-called denervation, produced by this section, leads to an increased sensibility of the structure to adrenalin which may be correlated with the uncontrolled action of these peripheral neurons.

The evidence afforded by the action of ergotoxin seems to indicate that adrenalin stimulates the endings of both augmentor and inhibitory nerves or the structure upon which each of these acts. Large doses of ergotoxin prevent stimulation of sympathetic nerves from producing their augmentor effect, but when inhibitory fibres are present, allow these to act. Adrenalin, administered after ergotoxin, produces inhibitory effects, when an inhibitory mechanism is present. Thus the conclusion is reached that it acts both upon augmentor and upon inhibitory endings.

The action of adrenalin on the termination of the augmentor nerves of the heart is masked by the action of the vagus. As the arterial blood-pressure rises, a reflex inhibition of the heart is brought about through the vagi. Only after these nerves have been cut, or thrown out of action by atropine, does adrenalin produce acceleration and augmentation of the heart. Dixon finds that large doses of apocodeine prevent stimulation of the augmentor nerves from acting on the heart, and also abolish the action of adrenalin, indicating that here too adrenalin acts on the special nerve terminations.

The law that adrenalin acts by stimulating the endings of the true sympathetic nerves is universal. It was first

definitely formulated by Elliot, and it may be called Elliot's Law.

In the eye, stimulation of the sympathetic in the neck causes dilatation of the pupil, retraction of the nictitating membrane of lower animals and opening of the eyelids by the non-striped muscle fibres in them. All these effects are produced by adrenalin. The action on the pupil becomes more manifest, if the superior cervical ganglion has previously been excised. This appears to leave the peripheral mechanism more sensitive. In this condition the mere instillation of adrenalin into the conjunctival sac dilates the pupil. The same thing has been described by Löwi as occurring in dogs when diabetes is induced by removal of the pancreas, and in some cases of diabetes in man. The conclusion has been drawn that the internal secretion of the pancreas exercises a checking effect upon the terminations of the abdomino-thoracic sympathetic—a theory which, as will presently be shown, has been applied to the regulation of the supply of sugar to the body.

The same increased susceptibility of the pupil to adrenalin has been observed in cases of Graves's disease. Possibly this is due to an activation of the endings of the nerve by the internal secretion of the thyroid. It may, however, be correlated with an increased amount of adrenalin in the blood, which has been described by some investigators in this disease ; or, both elements may be involved.

On the muscles of the alimentary canal, in the doses usually administered in experimental work, adrenalin produces the effect of stimulation of the true sympathetic ; it inhibits peristalsis, and stimulates the sphincters to contract. This result is produced by doses insufficient to cause a rise in the blood-pressure. Hoskin and McClure have shown that in very small doses it actually increases peristalsis.

Its action on the bladder is of special interest, since the innervation of this viscus is different in different animals. The bladder of the cat is relaxed by stimulation of the hypogastric nerves, while the bladder of the ferret is made to contract. Adrenalin causes relaxation in the former, contraction in the latter.

Adrenalin generally causes a very marked increase in uterine contraction. But the result varies with the condition

of the organ, and sometimes in the virgin uterus the usual dose causes relaxation. Stewart's observations seem to show that, while small doses increase the contractions, large doses may decrease them. These differences are probably due to the respective condition of the augmentor and inhibitory nerve endings in the organ at different times.

Adrenalin, at least in large doses, acts as a stimulant to the glands supplied with fibres from the true sympathetic. This is well seen in the salivary glands, and it has been observed as well in the glands of the stomach.

On the kidney, the effect in constricting the vessels leads to a fall in the secretion of urine. But this is followed by a marked dilatation of the arterioles, and by a diuresis which may be entirely due to the vascular condition or may be in part determined by a stimulation of secretory activity.

The sweat glands, which are supplied by the true sympathetic nerves, are not manifestly stimulated by adrenalin. This is either a divergence from the general law, or is due to the contracted condition of the blood-vessels, preventing the manifestation of the secretory activity.

Not the least interesting effect of the administration of adrenalin is the appearance of sugar in the urine (glycosuria) due to an increase in the amount in the blood (glycæmia). This is most readily produced by subcutaneous or by intraperitoneal injection. It may also be caused by slowly injecting a weak solution into a vein. Herter and Wakeman stated that it is most marked when the adrenalin is applied to the pancreas, and they thought it was due to a toxic action, preventing the formation of the internal secretion of that organ, which keeps in check the mobilization of sugar in the liver. But I have found that the effect is produced in the bird after the removal of the pancreas, while Doyen, Morel, and Kareff find that adrenalin increases the glycosuria in a depancreatized dog. Its action is, therefore, not upon the pancreas.

The liver is the great store-house of carbohydrates in the body. In it there is a rich plexus of nerves, formed by migration of neurons from the gut wall, being thus an extension of the splanchnic nerves. Stimulation of these fibres causes an increased conversion of glycogen to glucose, as was

first shown by the brothers Cavazzani, and more recently by McLeod and Pearce. Starkenstein has further shown that stimulation of the central end of the vagus causes glycosuria, even after removal of the supra-renals. The evidence thus seems conclusive that the liver is supplied by true sympathetic fibres, and that stimulation of these, either direct or reflex, causes the mobilization of sugar.

The general applicability of Elliot's Law of the mode of action of adrenalin renders it probable that it stimulates these endings in the liver, and thus induces the increased output of sugar. But while the administration of adrenalin in large doses thus directly stimulates these nerve terminations, the question, of whether the glycosuria which may be induced by such procedures as the puncture of the floor of the fourth ventricle of the brain is simply due to an increased amount of adrenalin in the blood acting in this way, must be considered. Undoubtedly, puncture does not produce glycosuria after removal of the supra-renals. This seems to show that the presence of adrenalin is essential. But McLeod and Pearce found that stimulation of the splanchnic nerve did not generally cause glycosuria, if the plexus of nerves going to the liver is cut.

Further, Trendelenburg finds that the amount of adrenalin in the blood after diabetic puncture is not sufficient to produce glycosuria. It would seem that, in the glycosuria produced by such nervous lesions as puncture, two elements are involved —first, the presence of adrenalin, and second the stimulation of the hepatic nerves; that, in fact, the adrenalin simply activates the terminations of the nerve, so that they respond more readily.

This conception of the part played by adrenalin in the onset of glycosuria leads to the consideration of the significance of the presence of adrenalin in the blood, and of its constant production in chromaffin tissue. Does it exercise a constant stimulating action on all the terminations of the abdomino-thoracic sympathetic? Does it play a part in maintaining the arterial blood-pressure? The consideration of what we know of its mode of action, when administered in large doses, seems to negative such an idea. It inhibits the gut in smaller doses than are required to constrict the arterioles; hence, we

cannot suppose that, in the small amount normally present in the blood, it can have any tonic constrictor effect upon the blood-vessels.

The evidence seems rather to point to the store of adrenalin present in the chromaffin tissue being available to activate the terminations of the nerves, so that, when any of the various groups of these nerves, which constitute the abdomino-thoracic sympathetic system, is thrown into action, a response may more readily be produced. It is of course quite possible that, when large quantities of adrenalin are poured from the chromaffin tissue, the direct stimulating action, observed when large doses are administered, may be induced.

Such a conception of the part played by adrenalin explains, too, the reason of the direct control by the nervous system of the output from the medulla supra-renalis. Dreyer and Tscheboksaroff found that stimulation of the splanchnic nerve increases its amount in the blood of the supra-renal vein. Cannon and De la Paz showed that, in the cat, fright caused an increase in the blood of that vein, and Elliot, more recently, was able to show that a condition with physical manifestations similar to those shown in "fright," which are produced in cats by such drugs as morphine, decreases the amount of adrenalin in the medulla supra-renalis, and that section of the splanchnic nerves prevents this. He also found that stimulation of the central end of such a nerve as the sciatic, and direct injury to the brain, acted in the same way.

Any stimulus which produces a protective reaction of the organism, be it of fright or flight, thus seems to induce an increased outpouring of adrenalin. To render such protective reactions most prompt and efficient, a rise of arterial blood pressure, a checking in the activity of the abdominal viscera, and—if the effort is sustained—an outpouring of sugar, which is the great source of muscular energy, are of advantage. By the activation of the nerve terminations by adrenalin, these are secured with the smallest possible divergence of nerve energy from the systemic muscular system to the abdomino-thoracic nerves.

An article on the chromaffin tissue would be incomplete without some reference to the possible relationship of the medulla supra-renalis with Addison's disease. But, since the

pathological changes in the supra-renals, which are the basis of this disease, probably always affect both cortex and medulla, it is impossible to say which of the symptoms are due to implication of one tissue, and which to the other. In all probability, the low blood-pressure and the visceral disturbances must be associated with interference with the supply of adrenalin, which may lead to a less ready response of the blood-vessels to the action of the vaso-constrictor nerves, while the general muscular weakness is probably related to the implication of the cortex.

THE ADRENAL GLANDS.

By T. R. ELLIOTT, M.D., F.R.S.

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CLINICAL knowledge with regard to pathological conditions of the adrenal glands, has, unfortunately, not yet been joined to the facts established by physiological research with such happy completeness as to give that reward which all workers ardently desire, the power to control and check disease. Sooner or later the gift will come. But, in the meantime, the story of what has already been ascertained is to the physiologist of intense interest. It shows to him a new type of interaction in the body, in which the power of a special department of the nervous system is supported by, and, indeed, depends entirely for its continuance on, the secretion of a mass of cells which appear to belong to the system of the ductless glands. That conception may later prove to be one of wide-reaching application. It may be a master-key to unlock the dark chambers of other parts of the great nervous system of our bodies, and reveal in their intricate machinery as well the constant need for some energizing substance, supplied from a cellular secretion which wards off neurasthenic failure.

In addition to this definite and certain relationship, there arise half-solved problems of the meaning of the cortex of the gland, and its curious relationship to the other ductless glands and to the sexual development of the body. Much is still unknown. The investigators of this new country are still moving forward independently along the tracks of physiology, pathology, and clinical observation, so that it is as yet impossible to chart their discoveries entirely on the map of clinical medicine. Each must for the present be described separately, and it will rest with some later writer in THE PRACTITIONER to give the whole connected tale.

PHYSIOLOGY AND MORPHOLOGY.

The adrenal gland is built up of two entirely different

tissues. Its medulla is composed of semifluid cells, that lie embedded in a rich venous plexus. These cells secrete adrenalin, and when heavily loaded with this substance they take a yellow brown stain with chromate salts, from which they have acquired the name of chromaffine cells. Variations in their activity are indicated by the depth of the chromaffine tint.

Surrounding them is the mass of cortical cells, firmer, and loaded with a peculiar fatty substance, a doubly refractive lipoid which is their special secretory product. In addition to this is a brownish pigment material, which appears to an enormous extent in the guinea pig, but which apparently has nothing to do with the pigmentation of Addison's disease. The cortex forms in man at least 90 per cent. of the entire bulk of the gland, and it is the enlargement of the cortex which characterizes the adrenal glands of the higher animals.

An interesting fact in relation to this is, that in man the adrenal gland, up to birth, is relatively much larger than that of all other animals, and this enlargement is entirely due to an overgrowth of the cortex. But in the case of an encephalic fœtus, in which the body is perfectly formed, and the cerebral hemispheres alone are missing, then the overgrowth of the cortex also fails, and the glands are of a size entirely comparable with that found in the animals whose brains are so much inferior to that of man. This is the only fact which directly suggests that the cortex has anything to do with the nervous system.

The medulla, on the other hand, has very close nervous relations, with though a specially limited group, the nerves of the sympathetic system. This latter is that division of the visceral (autonomic) nervous system which originates – as was first shown by the brilliant researches of Dr. W. H. Gaskell, whose recent death English physiology now deplores – between the fore and hind limb plexuses, and supplies the vasomotor nerves and the inhibitory nerves of the intestine. Adrenalin has the remarkable power of stimulating only that plain muscle in the body which is supplied by sympathetic nerves, and the reaction produced by it is always identical with that caused by electrical stimulation of the nerves. The chemical substance circulating in the blood evokes exactly the same

response as does the nervous impulse. Each reinforces the other.

Further, it has been proved that the excretion of adrenalin into the blood stream is controlled directly by the splanchnic sympathetic nerves.[1] Any reflex or effort, whether it be in pain, fright, or quick, forced movement, discharges through these nerves a smaller or greater amount of adrenalin. Hurrying round in the current of the blood, this quickens the heart, constricts the blood vessels, and may even, as Cannon suggests, liberate sugar from the liver, and supply to the skeletal muscles a fuller amount of the food that they need in the stress of harder mechanical work.

Years before this was discovered, it had been shown by the morphologists that the adrenalin cell of the medulla is derived from the same tissue, morphologically, as the sympathetic ganglion cells. From this it follows, that the adrenalin cells and the ganglion cells are closely related stations on the great sympathetic highway from the central nervous system to the blood vessels. The adrenalin cell is essentially a part of this nervous system, and in reality not a peripheral gland cell at all. But it must not be concluded that its action lies in aiding the nerves directly. All the nerves of the sympathetic group can be removed from a cat,[2] and yet the animal will live and maintain a fairly satisfactory blood-pressure.

Removal of the adrenals alone causes death inevitably; for the muscle of the heart and blood vessels then loses its tone, and the blood-pressure falls lower and lower until at last the pulse ceases to beat. In a cat dying after excision of the glands, stimulation of the splanchnic nerves causes no rise of blood pressure. That, however, does not indicate a paralysis of the nerves as such. The fault is in the muscle itself, which can no longer contract even when stimulated directly by pituitary extract or other drugs. Only adrenalin can then evoke from it a rise in blood pressure; to all other stimuli, it is dumb. The other muscles and nerves of the body do not show a similar atonic paralysis.

From this, the deduction is clear. The adrenal glands, whether medulla alone or cortex and medulla, are concerned

[1] *Cf.* Elliott: *Journal of Physiology*, 1912. XLIV., p. 376.
[2] Elliott: *Brit. Med. Journ.*, July 15, 1905.

in maintaining the steady tone of all muscles innervated by sympathetic nerves. They are responsible day by day for the upholding touch that maintains the driving power of the pulsating current of blood by which we live. The nervous impulses, which play upon these muscles, merely serve to change the tension up and down, here and there, where special circumstances require more delicate adjustments to local and peculiar needs of the body.

Cortex.—The cortex is neither controlled by nerves nor morphologically related to them. Its cells are derived from a mass of tissue close to the kidney, in the neighbourhood where the sex-gland arises. As the latter, testis or ovary, descends to the pelvis it carries with it buds from this mass, which may be scattered along the line of descent and form accessory cortical adrenals along the spermatic veins. There is reason to believe that others are embedded in the sex-gland itself, giving rise to the lutein cells of the ovary or to the interstitial cells of the testis. By the latter cells are determined the sexual characteristics of the individual.

The cortical cells of the adrenals belong, morphologically, to a group of glandular organs, which are not in any way related to the nervous system, like the medulla of the adrenals, but are concerned in supplying some secretion which influences the growth and the reproductive powers of the animal. The thyroid and pituitary are probably members of the same ductless gland group placed at a higher segmental level.

So morphology gives the hint that the cortex may have some function of this nature: and, as will be seen later, there is certain and definite proof in clinical medicine of the existence of that mysterious power in occasional hypertrophic tumours of the adrenal cortex. Normally, however, the cortex does not seem to be concerned with these matters. Its cells are loaded in health with a fatty substance, built up chiefly upon a basis of cholesterin. This substance may be supplied to help the medulla to manufacture adrenalin, or it may have some entirely different function. It is not reduced in states of bodily starvation, even though the fat of the body elsewhere completely vanish. It disappears with great rapidity in all acute septic fevers, and frequently too as the result of severe hæmorrhage or fatal anæmias. It is often present to an excessive degree in advanced athero-sclerosis.

Recent work abroad has sought to correlate these changes in the cortical lipoid with those of the percentage of cholesterin in the blood. They do run closely parallel to one another. Although the question has not yet been analysed fully, the balance of evidence is in favour of the view that the adrenal cortex does not excrete cholesterin bodies into the blood, and so maintain this parallel rise and fall. It is more probable that the current runs in the other direction, that the cortical cells abstract the cholesterin from the circulation and use it for the higher metabolic purposes which that gland can alone achieve. The nature of these purposes is simply unknown. We may hope that more light will soon be thrown upon it from the work that has been initiated in the last two or three years on the entire cycle of cholesterin in the body, with its pathological perversion in atheroma, and in the formation of gall stones.[1]

ADDISON'S DISEASE.

Of this, the characteristic clinical features are the coldness, the flabby atony and weakness of the muscles, and the low blood-pressure. Pigmentation alone is never sufficient for the diagnosis, and the chief value of the pigmentation in a patient is that it serves to call attention to the need of considering the possibility of Addison's disease in the diagnosis of his case. The disease usually runs a rapid course in a few months, but it may, apart from special treatment, be checked even after the appearance of severe symptoms, and the patient may regain sufficient vigour to resume physical work for some years.

Soldier, discharged from army in 1902 with debility and Addison's disease. Until 1906, he remained an invalid with weakness and well marked pigmentation of hands and tongue. From 1907 to 1913, he worked at the Tower of London, cleaning rifles and even lifting heavy chests. He died in the spring of 1914, a typical case of Addison's together with spreading pulmonary tuberculosis. The adrenals were extremely atrophic and fibrosed, with only a few caseous areas. No accessories could be found. The thymus was enlarged, the thyroid small, and the pituitary was smaller than normal (·35 gm.).

All the symptoms, except the pigmentation, can be explained by the cardio-vascular atony and the paralysis of

[1] *Cf.* the review by McNee: *Quart. Journ. Medicine*, Oxford, 1913–14, p. 221.

the sympathetic nerves. The muscular weakness results from the poor circulation and impaired nutrition of the bloodless muscles. Œdema does not appear, because there is no obstruction on the venous side and the arterial pressure is so low. The tendency to vomiting and diarrhœa is probably due to an uncontrolled action of the vagus and other nerves in the failure of the sympathetic inhibitors. The heart-beat is extremely feeble, and therein lies the danger of sudden death. Any exertion or abrupt strain must be guarded against with sedulous care, lest it overtax the weakened heart. Warmth, complete rest, with light, nourishing foods, provide the chief means of treatment. The writer has used atropine for the vomiting, on the view that the sickness is caused by over-activity of the vagus, but no manifest good resulted.

Neither with animal experiments nor in man, has treatment with adrenalin been proved to be of value in prolonging life. I have used hypodermic and intravenous injections, of adrenalin without obvious benefit. Still, the substance is worth a trial. For hypodermic injection, the ordinary adrenalin chloride cannot be used for long, since its acidity tends to cause irritation at the site of injection. A freshly-made solution of adrenalin borate may be employed in doses of 1 cc. of 1/1,000 daily. The total amount of adrenalin in the two glands of a man is about 8 to 10 mgm., that is the equivalent of 150 minims of the 1/1000 solution. Probably, there is in health a daily consumption of from 50 to 100 minims, and it is practically impossible to supply this by intravenous infusion.

The tuberculous inflammation destroys the cortex of the gland as completely as it does the medulla. Experiments have not proved conclusively whether it is the cortex or the medulla that is essential for the maintenance of life. Every attempt, therefore, needs to be made to find out whether some other extractive of the gland in addition to adrenalin cannot be used for a more successful treatment of Addison's disease. Glycerine extracts of an entire bovine gland given by the mouth have proved, in my experience, to be no better than adrenalin itself. But it should be noted that it has been claimed that cats have been kept alive after the extirpation of both adrenals by the daily intraperitoneal

injection of cholesterin, the substance which forms so large a percentage of the lipoid of the cortex. According to Grigaut's analyses, there is no diminution of the cholesterin in the blood in Addison's disease, so that such treatment cannot logically be justified. Still it is worth a trial in man. The cholesterin may be given by the mouth as a 4 per cent. solution in olive oil; a gramme daily would do no harm. Yolk of egg and boiled brains might be included in the dietary on account of their high cholesterin content.

In the last three cases of Addison's disease which the writer has treated with hypodermic injections of adrenalin, the result of the first injection in each instance was a sharp rise of temperature, by two or three degrees. This temperature reaction to 17 min. adrenalin did not occur in other patients, and it is conceivable that further enquiry may prove it to be a useful test for Addison's disease, just as Cushing showed that defects in the pituitary gland cause the body to react to injections of pituitary extract by rise of temperature.

OTHER EXHAUSTING CONDITIONS.

Since the adrenal glands play such a leading part in the maintenance, day by day, of the tone of the heart and blood vessels, it is probable that they will be liable to acute exhaustion in states of fever and heart-failure. That has been proved to take place. Each gland of a healthy adult man weighs from 4 to 5 gm. Of this the medulla forms about 0·5 gm., and it yields on extraction 4 to 5 mgm., of adrenalin, that is 1 per cent. of its total weight.

I have published a series of measurements of the adrenalin load found in the glands of patients who died from various diseases.[1] In acute pneumonia, the gland is œdematous, fatless, swollen to twice its usual size, and the adrenalin load is reduced to 1 mgm. With other fevers, there is similar or less loss. Complete exhaustion does not occur. The greatest loss of all was found in afebrile cases of acute cardiac failure, such as the rapid and fatal dilatation that may arise in mitral stenosis, in which the patient with only too clear a mind feels with helpless anxiety the weakness that is conquering him, and cannot free his chest from the heavy sense of suffocation. Here the nervous system makes every effort to aid the

[1] *Quart. Journ. Medicine*, Oxford, October, 1914.

labouring heart. Through the call of the splanchnic nerves, adrenalin is poured out into the circulation, until at death the glands are almost completely empty. Their exhaustion is secondary to the heart failure.

Precisely the same is the case with the fevers, and with the fatal form of diphtheria that is associated with a low blood-pressure and hæmorrhages. In all these, the glands are not attacked first and chiefly. They are called upon to aid when the infectious diseases, attacking the body from different quarters, pour into it their poisons, and excite a general defensive reaction with fever, hurry of the heart, and so on.

We have long recognized the danger that presses nearer in pneumonia when the heart fails, and when the vasomotor centre loses its power to control and organize the defence. There is a third point of weakness, in the adrenal glands. The first two can be supported, by digitalis, or by strychnine. The third, which is more vital than any, we do not yet know how to assist. And the worst of it is that when the heart and blood vessels are weakened by the loss of the adrenal secretion, their tone is so altered that they can no longer respond to such drugs as strychnine or pituitary, which would incite them to fuller activity, if they were in a more normal condition. Logically, the treatment should proceed on such lines as are found beneficial in Addison's disease, but until we have learned how to deal with that condition of pure failure of the glands, it seems to the writer unwise to attempt to treat this third factor that leads to heart-failure in infectious diseases. Adrenalin has been employed in diphtheria and in pneumonia.[1] The results are doubtful.

Little need be said about the relationship of the glands on the other hand to states of high blood-pressure with atheroma and renal disease. French workers first suggested an overaction of the adrenals as a possible cause of a continued high blood-pressure. They have abandoned the view, but it is still advocated by some German and Austrian pathologists. As a matter of fact, there is no proof at all of either hypertrophy of the medulla or increased production of adrenalin in these states. The evidence with regard to this has been reviewed by the writer, in a paper in the October

[1] *Cf.* for example, Voigt: *Brit. Med. Journ.*, March 9, 1912.

number of the *Quarterly Journal of Medicine*. But many of the examples of high blood-pressure with arterio-sclerosis do show an hypertrophy of the cortex, the cells of which are abundantly laden with fat and project in irregular adenomata. In all probability, there is here some causal connection between the atheroma and the enlargement of the gland, but its exact nature remains unknown, and the uncertainty would forbid any attempt to treat the disease by removal of one adrenal.

Hæmorrhage into the adrenals is occasionally seen at the boundary zone between cortex and medulla. That which occurs at birth in asphyxia is of no special interest. Later in life, it is often associated with thrombosis in the main branches of the central vein, and the writer has seen it in septicæmia, in death from burns, in hæmorrhage from gastric ulcer, and especially in parenchymatous nephritis. No special symptoms are produced. In one case, both glands were destroyed by large hæmorrhages and thromboses about two days before death; yet no pain was complained of.

SURGICAL TREATMENT.

At present the surgeon is only asked to deal with tumours of the adrenal glands. The simple adenoma causes no phenomena. It is only recognized *post mortem*, and is then not infrequently mistaken for caseating tuberculosis. Of the malignant growths, the cancer from the medulla and the "hypernephroma," that arises either in the gland itself or from cortical islets in the kidney, are both so rapid in growth and dissemination that their eradication is generally hopeless by the time they have been diagnosed. Neither cause any features that may be ascribed to a special secretion, and they appear merely as soft, hæmorrhagic tumours.

There is, however, one type of growth from the cortex of the adrenal which develops very slowly and produces such characteristic changes that it can be diagnosed at a time when there is some possibility of a successful removal. These cortical overgrowths cause an early adolescence and sexual precocity, which is the very opposite of the juvenile giant with acromegaly.[1] The young male acquires hairs on the face

[1] *Cf.* Glynn: *Quart. Journ. Medicine*, January, 1912. p. 157.

and pubes years before his proper time, and his body at 9 or 10 years becomes that of a diminutive but strongly built man. The female, curiously, loses the characteristics of her sex, the menses cease, hair grows on the face, and her body slowly assumes a masculine contour. There is not of necessity any corresponding change in the emotional outlook of the individual.

This change slowly progresses and then—it may be years later—a painless tumour is recognized to be coming forward and inward above the kidney on one side or the other. The growth is not very malignant and secondaries are late. If the condition is diagnosed on the symptoms before the tumour is very easily palpable, then there is some hope that it may be removed successfully. The writer has, by the kindness of Dr. Gordon Holmes, seen such a case in which a perfectly normal young woman at the age of twenty lost her menses, as she thought after a fright. A beard commenced to grow, and the body assumed a masculine appearance. Four years later, a tumour of the right adrenal gland was removed. Time has not yet allowed of the development in this case of the hoped-for result, the return of femaleness, which will make the entire argument faultlessly complete.

Man, like most animals, bears the removal of one adrenal gland without any ill effects. The gland is occasionally removed by surgical misadventure in operations on diseased kidneys. This can generally be avoided, because the characteristic contour of the gland may be quite well recognized by palpation, as it lies on the side of the vertebral column above the upper pole of the kidney. Heavy handling of the gland, did in one instance that came under the writer's notice, cause its complete destruction by hæmorrhage. It is important that surgeons should be familiar with the position of this gland, and avoid injury of an organ that is of such vital importance.

THERAPEUTIC USES OF ADRENALIN.

These need a separate enumeration, for their value has been established by clinical observation and, like so many of the useful facts of medicine, does not at once flow from the guiding generalisations of pathology.

The artificially synthesized drug, which is now supplied by

many chemists, provides a solution, according to the formula adrenalin ·10, chloroform ·50, sodium chloride ·90, diluted hydrochloric acid ·28, distilled water to 100, which is slightly acid, and can be kept for at least a couple of months without loss of strength. A reddish brown tint or a precipitate indicates a deterioration, which requires the solution to be thrown away.

Hæmostatic.—Adrenalin causes a slight increase in the coagulability of the blood, but its chief action is that of local vaso-constriction. This is seen to greatest advantage in its use to allay the reddening of an irritant conjunctivitis. It must be applied *directly* to the area of bleeding or inflammation. Since the effect can only be produced where there are sympathetic vasomotor nerves, it fails in the lungs, in the brain, and in the spinal cord. Adrenalin is harmful in pulmonary hæmoptysis, since its effect, if any, would be that of raising the systemic pressure and driving a faster current of blood through the lungs.

Though useful in conjunction with novocaine for local infiltration anæsthesia, it should not be employed for analgesia by spinal injection, because there it does not cause that local vaso-constriction which would limit and prolong the action of the stovaine, and moreover it is directly poisonous to the cells of the spinal cord.

Upon inflamed tissues it has much less local action, and should not be used freely on account of the danger of rapid absorption by the dilated vessels. A healthy man will tolerate a hypodermic injection of 20 minims of the 1 : 1,000 solution without discomfort or resultant glycosuria, but if some of this chances to enter a vein there is immediate malaise, headache, and even sickness. The use of adrenalin in an ointment for internal administration to an inflamed urethra is not advisable. Though so beneficial in congested states of the mucous membrane of the nose or eye, it cannot be employed with the same advantage in the urethra, because it causes a lasting spasm of the urethral plain muscle.

The experimental observations of Goodman Levy[1] have revealed a danger in the use of adrenalin, that was previously unsuspected. A heart that is slightly under the influence of

[1] *Heart*, IV., p. 320, 1913.

chloroform is in a very unsteady state. Like a drunken man, who can walk but tumbles if he tries to run, it is liable, if urged to acceleration, to break into an irregular faster beat which may suddenly lapse into complete ventricular fibrillation, with diastole and death. Abrupt and fatal heart failure under light chloroform has undoubtedly been caused in this way by the absorption of adrenalin from the internal surface of the nose to which it had been applied in the course of an operation. Adrenalin should not be used where chloroform has been given.

Restoration in Shock.—The heart is accelerated and stimulated by adrenalin in a manner that is entirely natural, for it is a stimulus that is continually being applied from the adrenal glands themselves. The stimulus is transient, but it is often sufficient to establish on a better level a circulation that has fallen to a dangerously low degree in collapse from a lengthy operation. Pituitary extract can be given hypodermically, and its effect is prolonged. But adrenalin must be used by intravenous injection, with a pint of normal saline containing 15 to 20 minims of the 1 : 1,000 solution. Its restorative influence on the heart is much greater than that of the pituitary extract. Like the latter, it produces constriction of the uterus, but only for a brief time; consequently it has no value in labour cases.

Addison's Disease.—The use of adrenalin in this condition and in the acute exhaustion of the glands by fevers or fatigue and by emotional strain has already been discussed. It is unsatisfactory at present. But the temperature rise produced by it may prove to be a useful test for disease of the adrenals.

Diabetes.—Otto Lœwi suggested a test to determine whether a particular case of diabetes is of pancreatic origin or not. A few drops of 1 : 1,000 adrenalin are instilled into the conjunctival sac. If the pupil dilates more fully than that of a control case, the pancreas is at fault. The theory underlying this is too complex to be worth discussion. Some writers have been satisfied with the test; in my hands, it has proved to be inconstant and unreliable.

Hypodermic injections of adrenalin cause glycosuria in normal animals; and it is probable that in this way the nervous system uses the path through the adrenal glands in order to

mobilize sugar from the liver when this is suddenly required for muscular work. To my surprise, I found in one case of advanced diabetes that injections of 15 minims of adrenalin always caused a fall in the sugar excretion.

Asthma.—The great relief experienced in acute attacks of asthma as the result of hypodermic injections of adrenalin is a purely empirical discovery in medicine. It is a good illustration of the manner in which medicine is aided by those who try things, and do not wait to move until the step is completely justified by a formal theoretical explanation of the benefits expected to accrue from it. Doses of 1 to 6 minims can be given hypodermically. The benefit, if it comes at all, is felt in a few minutes. It is not due to the trace of chloretone, with which the solution is often prepared.

There is little reason to believe that repeated injections may cause harm by leading to atheroma, since the substance does not enter the blood vessels so rapidly as to cause a rise of blood-pressure. The muscles of the bronchioles are constricted by the vagus, relaxed by the sympathetic nerves. Hence atropine derivatives are useful to weaken the first control, while adrenalin promotes the action of the second. The amount that is absorbed is very slight, but it seems to be sufficient, and naturally it may be of value, whatever the exciting cause of the asthmatic reflex. For the so called "asthma" of renal disease, which is really a dyspnœa caused by acid changes in the blood, and is rarely associated with constriction of the bronchioles, the drug is useless and even harmful. The distinction should be carefully observed.

PLURIGLANDULAR INSUFFICIENCY: ITS INCIDENCE AND TREATMENT.

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PLURIGLANDULAR insufficiency, or hypoendocrinism, is a comparatively recent term, rarely found in the medical literature published seven or more years ago. To appreciate the full import of the subject which has been allotted to me, it is necessary, first, to realise the fact that the endocrinic system is a very essential part of the organism, since by its various internal secretions practically the whole of the workings of the body are regulated and correlated.

In his comment in the *New York Medical Journal*[1] on the advanced position taken by a Committee appointed by the Congresso della Società Medica Italiana in 1912, the editor says: "One cannot but be impressed by the vast field which the ductless glands have steadily invaded, in keeping with the conclusions announced nearly ten years ago, in this country, that these organs were second to none in the body in their bearing upon physiology, pathology, and clinical medicine." The Committee representing these Italian investigators in their official report to the Congress[2] asserted that: "The internal secretions manifest an influence upon the anomalies of growth, morphology, and organic metabolism; on nutrition and inherent excitability of the nervous system; on resistance to infections and intoxications, as well as a preponderating rôle in the causation of dyscrasias and morbid temperaments." They also conclude that the equilibrium of the nervous system, the sympathetic in particular, may be regarded as maintained by the internal secretions and that in nervous diseases *per se* they act probably as indirect or predisposing factors.

The active principles of these internal secretions are now

generally called hormones, and we are beginning to realize that they are a factor of extreme importance in the regulation of metabolism. In the body every motive force is balanced by a retarding force and this nice balance is essential to health; hence if one or another of these factors gain the ascendency, or is diminished in activity, disorganization must naturally result and the extent of this disorganization can hardly be confined to the single area in which it is initiated.

The intimate relations of the secretions of the various endocrinous organs predicate pluriglandular disturbance as the result of an initial monoglandular disorder, thus explaining the dictum of Bayard Holmes[3]: "During the past year much evidence has accumulated to show that diseases of the ductless glands are usually plural rather than isolated and single. Pluriglandular disease is the rule rather than the exception."

Mullaly[4] states that from a study of the autopsy records at the Royal Victoria Hospital, Montreal, "In the infrequent autopsies in cases of ductless gland disorders pathological changes were observed in more than one of the ductless glands."

Functional disorders of many varieties may be either directly due to, or intimately associated with, changes in the various hormone stimuli which are so essential to the maintenance of the chemical balance upon which the intricacies of metabolism depend. Many of these disorders are already included in our present day classification of disease and are considered among "the disorders of the internal secretory glands," further discussed in this special number of THE PRACTITIONER. In most of these cases, however, the disturbance is prominent in one of the glands, and among these we recall thyroid insufficiency, the major form or myxœdema and the minor form, sometimes known as Hertoghe's syndrome (myxédème fruste), adrenal insufficiency or Addison's disease, Langerhansian insufficiency or pancreatic diabetes, parathyroid insufficiency or tetany, and numerous other disorders of function resulting from disturbance in the internal secretory activities of the gonads, hypophysis, epiphysis, etc.

Harry Campbell, in his masterly study of the rôle of the blood plasma[5] intimates that the blood plasma carries a host of varying chemical messengers or hormones whose balance

is essential to the proper regulation of the numerous bodily functions. This explains why the normal content of the chromaffin principle does not exert the same action as when a dose of adrenalin is administered—in the normal amounts in which it is found in the blood it is balanced by the Langerhansian principle.

Campbell considers that cell activity is properly divided into the egoistic and the altruistic cell functions. The former consists in the maintenance of individual cell activity, while the latter concerns the supply to the organism as a whole of certain services, probably brought about by the hormones, such as are exemplified in the numerous functional relationships between organs. This so-called "altruistic" function is of extreme importance, for the cell itself may seem to all intents and purposes quite healthy and yet still gravely fail in its altruistic functioning—a failure which, small though it be, may suffice to disorganize the delicate hormonic balance. A consideration of these complex interrelations[1] will establish the extreme importance of the hormone equilibrium, and, of course, its disturbances.

There are two forms of endocrinic disorder—organic and functional. The former, fortunately rare, is usually diagnosed only when the changes are permanent; it is, therefore, very difficult to treat satisfactorily. The latter, on the other hand, is extremely common, it is frequently overlooked, and, when its presence is appreciated and put under treatment, it responds in an encouraging way. Hence the principal effort of the writer will be to emphasize the frequency and importance of *functional* insufficiencies of the endocrinous organs, rather than the definite organic diseases of these glands. One can, however, advantageously refer, in passing, to several important papers and case reports which outline the pathology of those serious organic conditions which combine to form the "pluriglandular syndrome."

One of the most pronounced cases of organic pluriglandular disease was recently reported by Maase,[6] the essential facts being briefly recapitulated here. The patient was a Russian girl aged 24, with an epileptic and diabetic ancestry. Normal

[1] For a fuller discussion of this question, see Chapter III., "The Hormone Balance," in *Practical Hormone Therapy* (Baillière), by the writer of this article.

in every way till 18, she then developed ophthalmoplegia. At 20 she developed a myxedematous state attended by suppression of the menses. Glycosuria was found and a positive Wassermann reaction; later a spinal curvature was discovered. There was a shrinkage in the body measurements represented by various deformities. The bone condition somewhat resembled osteomalacia. Death occurred unexpectedly from erysipelas. At the autopsy the hypophysis, normal in size, was adherent to the bone and of firm consistence. Thymus remains were quite abundant, while the thyroid was abnormally small in both lobes. The pancreas was small, consisting largely of fat and connective tissue. The ovaries were abnormally small and showed no Graafian follicles. The bones were much thinned and brittle, the liver was fatty. The adrenals alone of all the endocrinous glands were normal, so that the case may be termed subtotal. The other organs were normal, save that the heart exhibited the changes to be expected after death from erysipelas.

In the Italian medical literature of the past year Consolazio,[7] Bianchi,[8] and Zilocchi[9] have contributed interesting monographs on this subject. In France, Costa[10] and Rebattu[11] have discussed this subject, and Parhon and his associates[12] have experimentally produced conditions in animals allied to the pluriglandular syndrome. All of these communications consider the serious organic conditions, and while there is undoubted advantage in studying this subject, it is of far less immediate practical value than the consideration of the much more frequent functional disturbances which, because of their insidious onset, are frequently entirely overlooked.

Costa[10] states that nice distinctions between conditions due to the various ductless gland disorders are very difficult to make, since the internal secretory glands all have an action on the development of the skeleton, on nutrition, and also a pressor or depressor action on the circulation. He does not attempt the differentiation suggested by Claude and Gougerot,[13] Gandy, Deséglise, and others, to determine in which gland the hypofunction predominates and which is essentially responsible for the disturbance. This undertaking appears to him much too difficult at present. In this case, however, the discovery of the cause was made by the Wassermann test

and antisyphilitic treatment caused a marked change for the better.

The majority of the serious organic disturbances of the ductless glands seem to be syphilitic in origin. The case reported by Costa above was luetic. In Maas's case, which has already been quoted, there was a positive Wassermann reaction, and de Moraes and Pernambuco,[14] in considering the relation of the pluriglandular syndrome associated with dementia præcox in a girl of 19, established the cause as inherited syphilis. They found that the ovaries, thyroid, adrenals, and mammæ were simultaneously affected.

The only reason that we study disease is that we may be the better able to appreciate its influence and satisfactorily treat it, so the consideration of pluriglandular insufficiency would be incomplete without reference to the treatment of these conditions. The natural corollary of pluriglandular insufficiency is pluriglandular therapy, and the most practical consideration of this subject concerns the comparatively recent form of therapeutics which the knowledge of the influence of hypoendocrinism has made possible.

It is altogether possible that the change of air ordinarily recommended to convalescents and invalids, sanatorium treatment and other hygienic regimens, are beneficial largely because of the increased activity of the secretory capacity of all the glandular organs and it seems that the tonic physical measures, such as hydrotherapy, electricity, massage, etc., are useful in part at least because they stimulate the endocrinous organs to produce their vital messengers. In fact, Nogier[15] has suggested a special line of treatment with the hope of specifically exciting the internal secretory organs by physical methods, just as these methods are used to stimulate other functions, thus materially modifying the conditions due to hypoendocrinism. This may be good, but cannot be compared with the organotherapeutic methods.

The most natural means to favour internal secretory activity are the products of the internal secretory glands themselves. Hallion's law is the fundamental basis of scientific organotherapy. It is as follows:—"Extracts of an organ exert on the same organ an exciting influence which lasts for a longer or shorter time. When the organ is insufficient, it is con-

ceivable that this influence augments its action, and, when it is injured, that it favours its restoration."

One of the most important statements on the hormones is found in Starling's monograph on "The Chemical Co-ordination of the Body Functions."[16] This eminent authority confidently states his belief that "if the mutual control of the body be largely determined by the production of definite chemical substances in the blood, the discovery of the nature of these substances must enable us to interpose at any desired place in these functions, and by this means to acquire an absolute control over the working of the human body. Such a control is the goal for which medical science must ever strive."

Possibly, the not infrequent cases of seeming monoglandular disorder which do not respond to the orthodox treatment whether organotherapeutic or otherwise, might be more responsive if the fact that pluriglandular disease is much more common than monoglandular disease was considered, and the administration of suitably combined extracts was substituted for the present thyroid, pituitary, adrenal, ovarian or other single extracts which may seem to be the proper treatment.

It is quite certain that this subject, now on the verge of our present knowledge, before many years have passed will be taken into careful consideration by the general practitioner as well as the internist, and the hormone balance will be much more thoroughly appreciated. It is true that the goal referred to in Starling's quotation is still far distant, and we are a long way from acquiring "absolute control over the working of the human body," but there can be no reasonable denying that the administration of certain organic extracts makes possible a control over certain functional conditions that it is not obtainable in any other way.

For several years the writer has been studying the application of various combinations of pluriglandular extracts in pluriglandular insufficiencies, particularly in the so-called "run-down" conditions, where no positive evidence of any defective action of the gland or series of glands can be demonstrated. Such cases include many forms of neurasthenia and functional neuroses, and it is obvious that in the majority of these cases there must be a disturbed endocrinism. It is

hardly reasonable to suppose that in an individual with prominent manifestations of half-speed function, such as constant fatigue on slight exertion, defective oxidation as evidenced by low urinary solids, nerves that are easily set "on edge," circulation that is poor, with cold, clammy extremities, and not infrequently reduced tension and ambition, and mental powers much below par, that the production of the essential chemical messengers is not reduced just as are all the body activities. This being the case, pluriglandular therapy not only serves to replace, in however slight degree, the missing secretions, but favours an increased production of them by the homostimulant action already referred to.

Theoretically this sounds very plausible and practically it has been found to work very nicely. Pluriglandular therapy is undoubtedly empirical, for in the class of cases under discussion at least, there is no definite proof as to which of the ductless glands is deficient and to what extent. For this reason it has been ridiculed by some who forget that nine-tenths of our present therapeutics was at one time purely empirical, while a good share of it still has no positive scientific basis. A procedure that has secured results before may do so again, hence it is worth trying. This is the present position of pluriglandular therapy, and it is believed that the successes already obtained are an earnest of what is in prospect.

Several combinations of organic extracts have been tried experimentally, and from a considerable experience it seems that the really tonic principles of this character are to be secured from the pituitary body, thyroid and gonads. My experience has been limited to the use of combinations of the extracts of the ductless glands which are known to have a tonic effect. Chief among these are the thyroid, posterior lobe of the pituitary and gonads, and for the past two years I have used a preparation called hormotone with excellent results in a variety of "run-down" states, in some of which there were obvious disturbances of one or more of the ductless glands and in others in which this change was not so evident.

Leonard Williams, whose studies in this field are of considerable interest, reported to the therapeutical section of the Royal Society of Medicine[17] that he had found that

while pituitary substance had given good results in those "curious and indefinite conditions—neurotic or neurasthenic—which occur so frequently in moth-eaten maiden ladies who emerge from boarding houses to go to church—I do not know how it does it, but it makes them feel better—. . . . . Since I have been using a mitrailleuse called hormotone I have had considerable success in those cases just referred to as benefited by pituitary." Among the conditions which I have treated are neurasthenia (in men and women), amenorrhea, sexual neuroses and impotence, as well as several cases in which the manifestations were not sufficiently marked to be definitely named — the "run-down" conditions.

This treatment is by no means a specific, and my percentage of good results is only between 60 per cent. and 70 per cent. I have seen no really bad effects, the only untoward effects occasionally noted being a feeling of irritability and temporarily increased nervousness, which disappeared on reducing the dose of hormotone and did not reappear when its administration was very gradually increased.

In senile conditions and old age there is an invariable pluriglandular insufficiency due to the progressive decline in all the functions. Lorand, whose book on this subject [18] is practical as well as interesting, makes frequent reference to the value of organotherapy, and I must admit that, in a number of cases which have come to my attention, the combination previously referred to has seemed to rekindle the vital fires.

The advantages of pluriglandular therapy are essentially the advantages to be derived from the individual substances which are combined. Obviously such combinations are made with their synergistic action in mind. I have personally used small doses of antagonizing extracts with good results, because it seems that each of the substances stimulates the corresponding organs, thus increasing the hormone content of the blood as a whole and strengthening the chemical messages which are of such vital importance. A point worth emphasis concerns the capacity of the individual organ to respond to the stimulus of the corresponding extract. It seems established that "the degree of stimulation exerted by the administration

of the hormone-bearing substances is in direct ratio to the need for such stimulation, *i.e.*, an extract is more efficient when a corresponding active principle is deficient in the body than when present in normal amounts. Hence in a combination of several extracts the principal action is the one which is deficient ; that is to say, the more it is needed, the more useful it is." [19]

Before closing it is proper to mention several reports in the literature of various forms of pluriglandular therapy. In addition to the treatment of the definite thyro-pituitary deficiencies with thyroid and pituitary extracts, as first suggested by Rénon and Delille,[20] Starkey [22] has been treating certain nervous diseases with a combination of thyroid, parathyroid, testis and ovary. Bazzochi [22] has used a combination of thyroid, thymus and spleen in pyloric cancer. In pharyngeal carcinoma, Shirlaw [23] suggests the use of the preparation called "*Tabloid three glands,*" each tablet containing a large dose of thyroid (6 grains) with the addition of small doses of adrenal and pituitary substances. Unquestionably in cancer there is a definite hypoendocrinism, and attempts to modify this, while possibly without specific effect upon the cancer itself, may be of assistance in modifying other conditions which cause inconvenience to the patient.

"Cancer is essentially a disease of nutrition—*i.e.*, errors in nutrition, whether local or general, are the factors which permit of the implantation of cancer cells and the growth of the tumour. The ductless glands preside over nutrition. Hence it is not unreasonable to suppose that there may be some relation between disturbances of the hormone balance and cancer, and, too, that there may be some prospect of therapeutic value in the treatment of this disease by organotherapy." [24] Finally, Billard [25] has advocated a combination of the extracts of spleen, liver and pancreas as an adjunct remedy in cancer.

Altogether the possibilities of various pluriglandular combinations are almost without number, since, as Leonard Williams [17] has indicated, the mitrailleuse is seemingly more useful than the single rifle shot.

Since this was written Little [26] has made another interesting communication on his study of cancer, and shows that not only must we consider the relation of the ductless glands and their

disorders to cancer, but that the use of certain products of these organs has a decided effect in favouring the response of the body to other treatment. He used extracts of the pancreas and adrenal cortex. Little's hypothesis has several important points which are worthy of repetition: The probable origin of the growth is in a highly specialized cell or cells, which for some reason or other have undergone a retrograde metamorphosis to the point where the power of reproduction, common originally to all cells but lost in these highly specialized cells, has reappeared. This reproduction of such reverted cells is caused by a relative hypofunction of certain ductless glands. The ductless glands at fault in each case have some vital relation to sugar metabolism or calcium metabolism or both.

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THE FUNCTIONS OF THE PITUITARY BODY.

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[With Plate XXXIV.]

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INTRODUCTION. OLDER VIEWS AS TO THE FUNCTIONS OF THE PITUITARY BODY.

The oldest theory concerning the pituitary body is transmitted by, and survives in, the name the organ bears. The secretion of the mucous membrane of the nose (pituita) was supposed to be derived from the "glandula pituitaria." This was the view of Galen, held also by Vesalius. At the period of Vieussens and Sylvius, the body was supposed to have to do with the formation of the cerebro-spinal fluid.[1]

Cushing calls attention to a remarkable paper by Lower ("Dissertatio de Origine Catarrhi," 1672), who was the first experimentally to disprove the Galenic doctrine. "For whatever serum is separated into the ventricles of the brain and tissues out of them through the Infundibulum to the Glandula pituitaria distills not upon the palate but is poured again into the blood and mixed with it."

Majendie regarded the pituitary as a kind of lymphatic gland, which collects the cerebral lymph and passes it into the circulation. "Its pars anterior does discharge its elaborated products into the circulation, and the pars nervosa apparently contains certain inter-neurogliar spaces resembling lymph channels" (Cushing, 43).

For a long period, the pituitary body was looked upon as a "vestigial relic," and of no importance in the animal economy.

The association of Addison's disease with adrenal lesions was the starting point of adrenal physiology, and the connection between myxœdema and thyroid mischief was the beginning of our knowledge of the functions of the thyroid. In the same way, the appearance of Marie's publications (1888–1889) on acromegaly and pituitary tumours, was the chief impetus towards all the modern investigation into the structure and functions of the hypophysis cerebri.

Of supreme importance in the history of our knowledge of the pituitary, as indeed of all the ductless glands was the discovery by Oliver and Schäfer (1894) of the

[1] It is interesting, as pointed out by Cushing (43), to note that a substance from the gland may under certain conditions enter the nose, and that, according to modern conceptions, the pituitary body does add something to the cerebro-spinal fluid.

PLATE XXXIV.

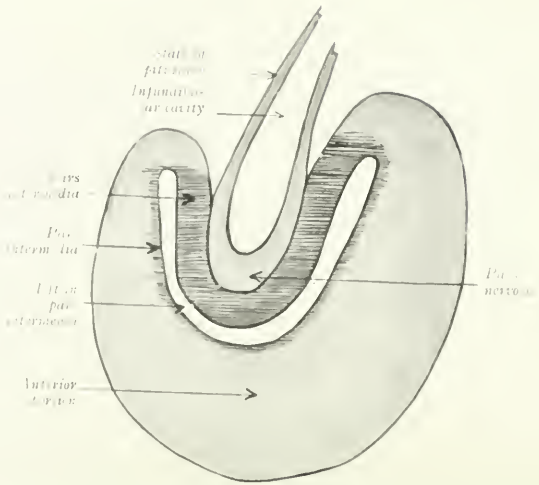

Fig. 1

Fig. 2

physiological activity of adrenal extracts. This led directly to the observation by the same authors of the power in raising blood-pressure of extracts made from the pituitary body, and has instigated a vast amount of work depending on the investigation of the action of various tissue extracts upon the body generally and on the different systems.

A.—BRIEF ACCOUNT OF THE STRUCTURE OF THE PITUITARY BODY.

The pituitary body consists of three parts, viz., the pars anterior or pars glandularis, the pars intermedia, and the pars posterior or pars nervosa.

The pars anterior is derived from the ectodermic wall of the buccal invagination, known as "Rathke's pouch." The pars posterior is a downgrowth from the thalamencephalon. The pars intermedia appears to arise secondarily, though at an early period, from the pars anterior.

In many animals, there is a cleft in the pars intermedia, and when a rough anatomical separation into anterior and posterior lobes is made, there is a layer of pars intermedia adhering to the posterior lobe, and a thinner layer of this portion remaining attached to the anterior lobe. (*See* Fig. 1.)

The anterior (glandular) portion is made up of a branching compact network of epithelial threads and columns. In the interspaces of the epithelial network run wide, thin-walled blood-vessels, so that in many cases the epithelial cells are placed directly on the delicate vessel-wall. This arrangement is most admirably adapted for the purposes of internal secretion. The general scheme of structure is the same as in the adrenal cortex, the islets of Langerhans, the thyroid apparatus, the thymus (in its epithelial stage), the interstitial tissue of ovary and testis, and the corpus luteum. The general nature of the cells found in the glandular pituitary may thus be stated:—

1. Chromophile { *a*. Acidophile / *b*. Basophile
2. Chromophobe.

The intermediate portion consists of finely granular cells, and is almost devoid of blood-vessels. Colloid material

occurs between the cells of the pars intermedia, and is sometimes contained in definite vesicles resembling those of the thyroid. The colloid material, however, is not of the same kind as in the thyroid, for it contains no iodine, though the vesicles are increased in number and size after thyroidectomy.

The pars nervosa is composed of neuroglia of a primitive type, and contains granules and masses of a hyaline substance derived from the pars intermedia. The nervous portion also contains pigment cells and granules[1] (Figs. 1 and 2, Plate XXXIV.).

B.—PHYSIOLOGICAL ACTION OF EXTRACTS OF THE PITUITARY BODY.

1. EFFECTS ON THE HEART AND BLOOD-VESSELS.

In 1895, Oliver and Schäfer (189) found that extracts of the pituitary body give rise on intravenous injection to a marked rise of the general arterial blood-pressure. The rise is comparable to that produced by extracts of adrenal medulla, but is more prolonged.

Howell (143) found that the substance, which produces the rise of blood-pressure, is confined to the posterior lobe of the pituitary body. He further noted a slowing of the heart's action, and the fact that, if a second dose be administered within a certain time after the first, these effects are not repeated—in other words, a certain degree of immunity is established, which only slowly passes off.[2] A second dose is followed by a fall, not a rise, of blood-pressure. (Schäfer and Vincent, 226 and 227.)

Cyon (46), as well as Howell, observed that the rise of blood-pressure is accompanied by slowing of the pulse. The former writer attributes these effects to stimulation of the pituitary body by the extract which has been injected (Cyon, 47). He states that stimulation of the pituitary body *in situ* will produce the same effects, which are, on the other hand, not obtained by injections into an animal from which the

[1] Edinger (71) gives an interesting account of the structure of pituitary secretory cavities, which communicate with the perivascular spaces of the brain. For a further account of the pigment in the nervous hypophysis *see* Kohn (149) and Vogel (258).

[2] At this time, Szymonowicz (244) was unable to obtain similar results.

pituitary body has been extirpated.[1]

There is slowing of the isolated mammalian heart, if extract of the "posterior lobe" be perfused through it (Cleghorn, 31; Hedbom, 116).

We have seen that Schäfer and Vincent, working with cats, found that pituitary extract, on administration of a second or third dose, always produces a fall, and not a rise, of pressure. The depression substance was subsequently shown, by the present writer and collaborators, to be common to extracts of all organs and tissues.[2]

Osborne and Vincent (191), working with dogs, found, with Howell, a preliminary fall before the rise, but, in most cases, a rise as well as a fall on a subsequent injection. This is what I have observed in a recent series of experiments.[3]

The main facts have been found to hold good as well for extracts made from the human pituitary (Halliburton, Candler, and Sikes, 109).

According to Schäfer and Vincent, the cardiac slowing is not constant, and, when present, it is not abolished by section of the vagi or the action of atropine. It is, therefore, of peripheral origin, and is not due to the same cause as the inhibition which often accompanies the action of adrenin, and is brought about by an action on the cardio-inhibitory mechanism in the bulb.

This action of pituitary extracts upon the heart and blood-vessels is a special case of their action upon most of the involuntary muscles. The rise of blood-pressure already referred to is due to constriction of many of the blood-vessels of the body, combined with augmentation of the heart-beat.[4]

With large doses, the depressor effect may be so marked as to mask the usual subsequent rise (Silvestrini, 233, 234).

According to Howell, the responses become less and less pronounced with each repeated injection. There is great variation in the effects produced not only between different

[1] See, however, Section F. of this article; also Biedl and Reiner (17) and Schäfer and Vincent (226 and 227).

[2] See Vincent (257).

[3] In one experiment, even the first administration of pituitary extract produced no rise, and this result seems to have been due to the previous administration of adrenin.

[4] Paton and Watson (201) state that in the duck there is dilation of vessels and not constriction.

species of animal, but even between different individuals of the same species.

It has been doubted (Dale, 62) whether the depressor action, seen with injections subsequent to the first, is wholly due to a different principle, though the evidence before us seems to the present writer to be strongly in favour of such a view.

Hoskins and McPeek (127) discuss the question, whether the pressor effect of pituitary extract is due to adrenal stimulation, and come to a negative conclusion.

Experiments upon the isolated heart of the frog and of mammals show that the slowing of the heart-beat is due to a direct action upon the musculature of the heart (Hedbom, 116; Herring, 117). Einis (73) finds that the first effect of pituitary extract upon the heart is a diminution of the frequency, this is followed by an increase.

2. EFFECTS ON THE VASO-MOTOR REFLEXES.

The facts that adrenin diminishes the excitability of the vagus,[1] and that fluid from the thyroid appears to increase the excitability both of the vagus and the depressor (Cyon, 44 and 60; also Asher and Flack, 11), led to an investigation[2] of the action of these and other tissue extracts upon the vaso-motor reflexes.

The extract of the pituitary body, sold under different names by different firms, appears to convert a depressor reflex into a pressor, or very considerably to exaggerate the pressor effect. The latter effect is, in some cases, much more marked after previous administration of adrenin. This action of pituitary extract occurs only on a first injection.

Brisk kneading of the intestines evokes normally a very distinct vaso-motor response, which is frequently accompanied by a slowing of the heart-beat. The effect upon the heart is very noticeable after the administration of pituitary extract, and the beat is frequently of a grouped character.

3. EFFECTS ON THE RESPIRATION.

Mummery and Legge (184) have noted a diminution of

[1] This is not always the case; the precise conditions under which this occurs, require careful investigation. (*See* Vincent and Cameron [in the Press] also Vincent (257).)

[2] Vincent and Cameron. [In the Press.]

the amplitude of respiration, as a result of pituitary injection. Pantow (197) states that breathing stops for some time after the injection, then begins again, then once more stops; the primary stoppage appears to be due to peripheral vagus stimulation.

4. EFFECTS ON VOLUNTARY MUSCLES OTHER THAN THOSE OF THE VASCULAR SYSTEM.

(a) *The uterus.*—It was first recorded by Dale (61) that infundibular extract excites uterine contractions. The observation was confirmed by Bell and Hick (16), and v. Frankl-Hochwart and Fröhlich (90). As pointed out by Dale, the uterus is extremely sensitive to the action of the extract, whether in the body or treated as an isolated organ. Kehrer (145) first used the uterus in the latter way, and noted the action of pituitary extract upon it. Engeland and Kutscher (78) affirm that they have succeeded in separating, by a method of fractional precipitation, from an extract of the whole pituitary body a basic fraction possessing the characteristic action on the uterus, but not that on the blood-pressure. According to Dale and Laidlaw (63), the isolated horn of the uterus of the non-pregnant cat gives fairly good results, responding with but little diminished contraction to a second dose, after the first has carefully been washed away. It is subject, however, to inconvenient spontaneous slow variations of its average tonus, and is apt to acquire a disconcerting rhythm. The uterine horn of the young virgin guinea-pig is greatly superior in these respects, its natural tendency, when left undisturbed in the Ringer's solution, being to acquire a condition of complete relaxation, broken only by a small rhythm. It is very sensitive to the extract, which can therefore be given in very small doses, and the tissue normally relaxes with promptitude to its original level of minimal tonus on washing out and changing the solution. This method is found to detect differences of activity which escape recognition by the blood-pressure test, and is employed by Dale and Laidlaw for standardizing pituitary extracts. (*See also* Schiffmann, 230.)

(b) *The bladder.*—The action of pituitary extract on the bladder was first noted by Bell and Hick (16). In dogs and cats, pituitrin stimulates to a considerable extent the

musculature of the bladder, and increases the excitability of the pelvic nerve (Frankl-Hochwart and Fröhlich (90), and Hofstätter 124).

(c) *The intestine.*—Bell (15) observed the power of pituitary extract to restore peristalsis to the paralytically distended bowel, a capability which, according to Dale and Laidlaw, is not represented by any definite action on the bowel of the normal animal. But Beyer and Peter (13), working with the surviving small intestine of rabbits, find that, after a preliminary diminution in rhythm and tone, both these are very strikingly increased. The rhythmical movements are often increased tenfold. The first phase is considered by the authors to be due to stimulation of the sympathetic fibres which inhibit the muscle. The second phase, on the other hand, is due to stimulation of Auerbach's plexus and the post-ganglionic fibres. With very powerful doses, this second effect is very slightly manifested or may be absent altogether, so that an immediate and lasting inhibition may be the only result.

Just as Schäfer and Vincent found two separate substances acting on the blood-pressure—a pressor and a depressor—so Beyer and Peter distinguish two separate substances having respectively the two actions on the intestine just described, the sympathetic inhibitory substance being insoluble in alcohol, the autonomic augmentor substance soluble.

These effects on the intestine can be repeated at frequent intervals, while the effect on the bladder rapidly becomes less in successive trials.

It is doubtful how far these effects are truly specific for extracts of pituitary.

The effects of pituitary extracts on the intestine have been studied also by Ott (194), Foderá and Pittau (88), Franchini (89), and Houssay. The latter author has also recently given an account of some medical applications of these effects (136).

(d) *The stomach.*—The effects of pituitary extract on the stomach appear to resemble very closely those upon the intestine just described. There is at first some inhibition, which is followed by a powerful and persistent augmentation.

The rhythmical movements are very markedly exaggerated. These actions were first noted by Houssay in the frog, and then in other animals and man (131, 132, 133). The results were confirmed by Bonis and Midulla (18).

Clinical observations in the same direction were made by Udaondo (251) and Ibañez (144).

(e) *The pupil.*—It was discovered by Cramer (38) that pituitary extract dilates the pupil of the enucleated frog's eye. Franchini (89) noted also that the serum of animals which have received intravenous injections possesses slight mydriatic properties (*see also* Cattapano, 26).

There is thus a close resemblance between the reactions, due to administration of pituitary (posterior lobe, infundibular) extracts, and those so familiarly called forth by means of adrenin. The chief differences consist in the preliminary fall (in some animals) and prolonged rise due to pituitary, and the fact that this drug causes slowing of the pulse after atropine or section of the vagi, in the constriction of the coronary and dilatation of the renal vessels, adrenin having an opposite effect (Cushing, 43; Pal, 196).

5. EFFECTS ON THE SECRETION OF CERTAIN GLANDS.

(a) *The mammary gland.*– Ott and Scott (195) discovered that injection of pituitary extract into goats causes a marked increase in the flow of milk. Schäfer and Mackenzie (225) and Mackenzie (172) found that extracts of pituitary body, corpus luteum, pineal body, involuting uterus, and lactating mammary gland all manifest a galactagogue action, but the pituitary body produces the most marked results.

Gavin (101) found that the daily yield of milk in cows is not increased by the administration of corpus luteum and pituitary extract. Schäfer (222) also reports that injection of pituitary extract into a muscle of a lactating woman caused only a temporary increase in the flow of milk.

It has been suggested (Hammond, 114) that the hypertrophy of the mammary glands is brought about by some secretion produced during pregnancy, which neutralizes the tendency of the cells to discharge under the influence of secretion from the pituitary and other organs. When this

inhibitor is removed, the hormones causing the discharge of the gland come into action, and so cause the secretion (Hammond).

This seems likely from the experiments of Mackenzie, who states that, by injecting extracts of fœtus or placenta together with pituitary extract into a lactating animal, the action of the pituitary is inhibited. D'Errico (69) injected blood from a pregnant bitch into a lactating one, and found that milk secretion was inhibited, whereas blood of a non-pregnant bitch when so injected was inert.[1]

In regard to the corpus luteum, there is a theoretical discrepancy between the views of those who regard the body as one of the building-up factors,[2] and the results of Schäfer and others who find that corpus luteum extract produces an immediate secretion.

Hammond (114) finds, as did previous observers, that the galactagogue effect of pituitary extract is only temporary. The effect is not muscular. The daily yield is only slightly increased, and is not dependent on increased blood-pressure. The pituitary gland seems not to be the origin of the ordinary changes in the mammary gland. Histological evidence points to a direct action of the extract on the glandular epithelium. The milk obtained after injection has a higher percentage of fat than normal; in the subsequent milkings, however, there is a drop in the percentage of fat, although that of the other ingredients remains normal.

While the proteins, lactose, and ash are secreted in close connection with the water of the milk, the amount of fat is not so connected with the amount of water. The ratio of "nitrogen to lactose" is relatively constant throughout.

Houssay (142) has reached the same general conclusions as Hammond, though independently. The former observer lays stress on the temporary nature of the effect.[3]

(*b*) *The kidney.*—The diuretic action of pituitary extracts

[1] *See*, however, Mackenzie (172).

[2] O'Donoghue (187) and Vincent (257).

[3] Since the above was written I have seen the paper by Hill and Sutherland Simpson (*Quart. Journ. Exp. Physiol.*, 1914, viii. p. 103), who state that pituitary extract increases the immediate secretion of milk, but causes afterwards a decrease below normal

was discovered by Magnus and Schäfer (173), and a fuller account was given by Schäfer and Herring (224). The increase of secretion is accompanied by dilatation of the renal arteries, so that the organ swells. The action is, therefore, different upon the renal vessels from that on the arteries in general, which are strongly contracted by it (Schäfer, 223; Hallion and Carrion, 112). The rise in blood-pressure produced by this general contraction is not the sole cause of the increased secretion of urine, for a second dose administered a short time after the first will again accelerate secretion, although the second dose may not cause any rise of general blood-pressure, but rather a fall. There is, therefore, a specific diuretic effect upon the renal epithelium, just as there is upon the epithelium of the mammary gland (Schäfer, 223). The tolerance produced by a first injection is then less marked than in the case of the blood-pressure response, but with large doses it is well marked.

Beco and Plumier (14) report that, under certain circumstances, there is a secondary diminution of the flow of urine, following upon vaso-constriction of the kidney.

Hoskins and Means (126) believe that the pituitrin diuresis is due primarily to direct stimulation of the renal cells—usually aided, perhaps, by a concomitant vaso-dilatation in the kidneys.

(*c*) *The stomach.*— It was shown by Edkins (72) that extracts made from the pyloric mucous membrane in boiling water or 0·4 per cent. hydrochloric acid contain an active substance which, on injection into the blood-vessels of an animal, leads to a secretion of gastric juice.

Frouin (95) found a similar action on the injection of gastric juice. Eirenhardt (74) confirmed the results of Edkins, but Emsmann (77) obtained some definite effects upon the flow of gastric juice as a result of injection of extracts of other organs, such as the intestine.

Houssay (137) has recently reported a very decided action of pituitary extracts upon the flow of gastric juice, and has published some very convincing tracings. This appears to be a direct action on the secreting cells, as in the case of the mammary gland and the kidney. At any rate, the effect can

be observed upon the isolated stomach.

6. GENERAL PHYSIOLOGICAL EFFECTS (SUBCUTANEOUS AND INTRAVENOUS INJECTIONS).

In 1899, Schäfer and Vincent (272) reported that they had made a few experiments upon the effects which can be produced by the subcutaneous injection of decoctions of the infundibular part of the pituitary body. These were performed upon mice and young rats, and, although the dose required was much greater, showed that the pituitary extracts can produce results resembling in a general way those of adrenal extracts (Oliver and Schäfer, 188, 189; Vincent, 255). They cause quickened respiration, increased heart's action, and ultimately paralysis, beginning in the hind limbs.

Similar experiments have since been carried out by many observers. Etienne and Parisot (82, 83), Renon and Delille (210, 211), Azam (12), and A. Delille (65, 66, 67) have found diuresis as a result of injection of the extract, and Thaon (248) records hæmaturia and albuminuria. Etienne and Parisot (82) further record a permanent hypertension as the result of repeated injection of pituitary extracts. Mairet and Bosc (174) observed very little effect on subcutaneous injection (*see also* Panton, 197), while Carraro (23) succeeded in causing the death of rabbits by means of subcutaneous injection of pituitary extracts.

Conti and Curti (36, 37) state that the effects of subcutaneous injection are modified by previous injection of thyroid extract, or extract made from the anterior lobe of the pituitary body or the pharyngeal pituitary.[1]

The toxic effects of pituitary extracts are not nearly so pronounced as those of the adrenals. The symptoms observed, in addition to those mentioned above, are apathy and somnolence, excitation followed by muscular weakness, sudden cessation of heart-beat, and loss of weight after repeated injections, cardiac hypertrophy, ulceration, and hæmorrhages in the intestine (Franchini, 89), and hyperæmia and hæmorrhages in the kidney (Thaon, 247, and Giavedoni and Ruggieri, 104).

Urechia (252) found that a reinjection after an interval of

[1] Garnier and Thaon (100), and Salvioli and Carraro (216, 217) have also contributed to our knowledge of this subject.

ten days gave rise to symptoms of an anaphylactic nature (*see* also Panton, 197).[1]

C.—THE QUESTION AS TO WHICH ELEMENTS OF THE PITUITARY BODY FURNISH THE ACTIVE SUBSTANCE OR SUBSTANCES — FUNCTIONS OF THE DIFFERENT PARTS OF THE PITUITARY BODY.

As we have already seen, Howell (143) discovered that it is from the posterior lobe only that active extracts can be obtained. This was confirmed by Schäfer and Vincent (226, 227). The observation was contrary to what might have been expected, since, from the distinctly glandular nature of the anterior lobe, it would appear *à priori* that it would be more likely to furnish active physiological substances.

But we must remember that there are epithelial elements in, and in close relation to, the nervous portion (*see* Figs. 1 and 2), and it was a natural assumption that these, and not the nervous portion proper, would be found to yield the pressor substance. But some years ago, Professor Osborne and myself (191) tested the matter, and found that an extract made from the central part of the infundibular portion—devoid of epithelial elements—is much more active than one from the peripheral epithelial part. We expressed the opinion that probably the external layer would be found to be inactive if it could be obtained quite free from admixture with the central portion.

Schäfer and Herring (224) found this to be the case too with the substance which acts as a diuretic. Improbable, then, as it would appear at first sight, the conclusion is inevitable that it is the nervous portion proper which contains the substance or substances having such pronounced pharmacodynamical properties, different from those possessed by other kinds of nervous tissue.

Bell (15), Silvestrini and Badnel (235), Sandri (218, 219), Lewis, Miller, and Matthews (152) hold a different view, and have obtained different experimental results.

On the other hand, Foderá and Pittau (88), Salvioli and Carraro (216, 217) and Houssay (133), also Houssay and

[1] For recent work on the pharmacology of the pituitary body, *see* Fröhlich and Pick (92, 93 and 94).

Giusti (138) have obtained the same results as Osborne and the present writer.

I have never had an opportunity of repeating the experiments carried out in conjunction with Professor Osborne, but, since they have been confirmed by the above-mentioned writers, I am strongly inclined to adopt the view of Houssay that *the substance or substances are secreted by the cells of the pars intermedia, and then collected and concentrated, or changed into more active forms in the nervous portion proper.*[1]

No physiologically active substances can be extracted from the anterior lobe (except a depressor substance, which is common to all organs and tissues). This part of the pituitary is related to the general growth of the body, and especially of the skeleton. (*See* Section D.)

D.—FEEDING AND METABOLISM EXPERIMENTS.

The first metabolism experiments were performed by Schiff (229). He found that there was no influence on the nitrogen in any case, but that the phosphorus output was sometimes increased, due to katabolism of bony tissue. But, as pointed out by Malcolm (175), the increase may have partly been due to nuclein.

Moraczewski (182) found in a case of acromegaly the nitrogen output was increased, also that of phosphorus, while Oswald (193) found no effect on nitrogen or phosphorus.

Malcolm (175) noted that the anterior lobe, administered dry, tends to cause a retention of nitrogen; the dried nervous portion has a similar effect. The fresh entire gland, in large doses, increases the output of nitrogen. The anterior lobe causes a retention of phosphorus, while the posterior lobe causes a loss followed by retention. On the whole, Malcolm's results pointed to a greater activity on the part of the nervous portion.

Caselli (24, 25) observed no effect on growth from long-

[1] Herring (*Quart. Journ. Exper. Physiol.*, 1914, viii., pp. 245–274) has recently confirmed the results of Osborne and Vincent. "The pars nervosa is from two to five times more powerful than the pars intermedia in its action." He thinks that the substance acting upon the uterus is formed at an early stage in the pars intermedia, but the substance acting upon the blood-pressure and kidney is a later product, resulting from the breaking down of the hyaline bodies or disintegrating pars intermedia cells in the pars nervosa.

continued injections of extracts made from the whole gland, but in some cases feeding with the gland retarded growth. Sandri (218, 219) fed young mice and guinea-pigs with pituitary emulsion, and states that this caused an arrest of growth. Cerletti (27) injected pituitary emulsion intraperitoneally into young animals, and found that the animals receiving the injection fell uniformly below the controls in weight, and that the bones of the animals receiving the emulsion were, as compared with the controls, somewhat shorter as regards the diaphyses, but longer as regards the epiphyses.

Schäfer (220, 221) has carried out a series of feeding experiments on white rats, the general conclusion from which is that the addition of small amounts of pituitary tissue to the diet of rats has little or no effect upon growth.

Franchini (89), working with rabbits and guinea-pigs, reports that the calcium and magnesium metabolism is much reduced. Elfer (75) reports that subcutaneous injection of pituitary extract does not affect the protein metabolism, but induces a temporary retention of phosphorus, calcium, and magnesium.

Sack (214) says that the extract of anterior lobe of pituitary has no influence upon metabolism. [*See*, however, Mochi (179, 180, 181).]

Quite recently Rosalind Wulzen (261) has investigated the effects of administration of anterior lobe of pituitary body to young growing birds. A very distinct effect is shown in the direction of retardation of growth, which is manifested both in the body and in the length of the long bones. Involution of the thymus accompanies this retardation, and the suggestion is made that the former may bear a causal relation to the latter. The effects are more marked in males than in females.

In very few of these investigations (the last mentioned series forming a notable exception) has sufficient attention been paid to the difference between the anterior and posterior lobes of the pituitary. It must be pointed out that, even when ordinary care is taken to separate the anterior from the posterior lobe, the former will include a strip, which varies in thickness in different animals, of the pars intermedia.

The reflection of this part over the nervous portion is now well known, and account has been taken of its presence in the consideration of the effects of posterior lobe extracts (*see* Section C), but the fact which I have just pointed out, viz., that there is a reflection of the pars intermedia over the anterior lobe, is not so generally recognized. If the pars intermedia be traced round from the nervous on to the glandular portion, it will be noticed that the cells forming it gradually fuse with the cells of the glandular portion in the depth of the latter structure, but are continued as a layer, retaining at any rate some of the characters of the pars intermedia, along the edge of the cleft. Although the amount of pars intermedia adhering to the anterior lobe is not very considerable, it is possible that it might make a difference to the physiological extract.

Houssay (130) is the only author, so far as I am aware, who has definitely drawn this as a continuation of the pars intermedia; though Herring (118, p. 136) states that the anterior lobe in the cat is separated from the cleft by cells, "which are larger than endothelial cells," and are continuous at the anterior and posterior ends of the cleft with the cells of the epithelial reflection. He admits too that the cells of the intermediate portion occasionally spread down a little over the front of the anterior lobe. The general arrangements are shown in Fig. 1, and the microscopical structure in Fig. 2.[1]

E.—GRAFTING EXPERIMENTS.

The effects due to increased functional activity of the pituitary body cannot be induced by glandular transplantation (Cushing, 43). Cushing adopts the theory of W. S. Halsted (113) that an existing "physiological deficit" is one of the essentials for a successful organo-transplantation. In support of this, Crowe, Cushing and Homans (39) observed that the life of animals, after a total pituitary extirpation, could be prolonged by the immediate re-implantation into the cerebral cortex of the excised gland, which lived for a month.

In the absence of such a previously established deficit,

[1] Since the above was written two interesting papers on "The Influence of Thyroid and Pituitary upon Metabolism" have appeared (Hewitt, *Quart. Jour. Exper. Physiol.*, 1914, Vol. VIII., p. 103 and 295).

the transplanted gland becomes absorbed in a short time (Clairmont and Ehrlich, 30). In Schäfer's experiments (220), the only distinct effect noticed was with the posterior lobe, which caused a temporary increase in the flow of urine. As the implanted gland soon became absorbed, this result is probably to be looked upon simply as the effect of the administration of an equivalent amount of pituitary extract. It is possible, however, that the transplanted gland may have functioned for a short time.

In Exner's experiments (84) on rats, transplantations were made of glands taken from young animals, and there was a temporary increase in growth and weight. But it is possible, in this case as well, to assume that the effect was comparable to a long-continued administration of an equivalent amount of extract.[1] It is pointed out by Cushing that the results o these various transplantation experiments suggest some therapeutic possibilities for this method, as the slow absorption of the secretion may be an effective means of administering the active principle. Cushing appears to have obtained some clinical evidence that, when a patient is actually suffering from a physiological deficiency, fragments of a transplanted pituitary body may survive and remain permanently active.

F.—STIMULATION OF THE PITUITARY BODY *in situ*.

Cyon (46, 53) has studied the functions of the gland by the method of direct excitation. He exposed the hypophysis by trephining the base of the skull beneath the sella Turcica. Then he exerted light pressure upon the gland by means of a small pad of cotton. He observed immediately a considerable variation in the blood-pressure and in the number and intensity of the heart-beats. These variations occurred to some extent as the result of the trephining, but were much exaggerated by a very slight electrical stimulation. Cyon worked with rabbits, and noted a considerable slowing of the heart-beat, with increase of amplitude.

Different results have been obtained by Biedl and Reiner

[1] It must, however, be noted that the effects produced, viz., increase in growth and weight, are in a contrary sense to those observed by the majority of recent experimentors, administering the gland by the mouth. But the effect of giving whole gland would possibly be different from that of giving anterior lobe only. (*See* Section D.)

(17), Houssay (130), Caselli (24, 25), Gaglio (99), Pirone (206), Lo Monacho and Van Rynberg (168, 169), Livon (156), Collina (32, 33, 34, 35) and Lusena (171); but Masay (178) obtains results similar to those of Cyon, though his interpretation is different. The effect of direct stimulation of the gland he attributes, like Schäfer and Herring, to an increased discharge of the internal secretion into the blood-stream, where it produces the usual result due to the action of the extract upon the heart. The effect of ablation of the pituitary body, in abolishing the rise of carotid pressure on compressing the aorta (described by Cyon), is not easy to explain, though Masay is inclined to attribute it to operative shock.

Schäfer (220) reports that, in dogs, partial injury to the pituitary by means of a thermo-cautery or mechanical agents induces marked diuresis. This result is specially interesting in relation to the polyuria, which occurs in injuries and tumors affecting the base of the brain. This polyuria is more likely to occur when the pars intermedia is involved. [*See also* Rosenhaupt (213), Sternberg (241) and Borchardt (20).]

G.—EXTIRPATION EXPERIMENTS.

The first to perform experimental extirpation of the pituitary was Horsley (125), in 1886. Among the earlier workers must also be mentioned Friedmann and Maas (91), Lo Monacho and Van Rynberg (168, 169), Marinesco (176, 177), Vassale and Sacchi (253), Narbutt (185), and Gemelli (102, 103). These observers obtained contradictory results; but it was established by Paulesco (202, 203), in 1906, that the organ is essential for life, and that the onset of the acute symptoms depends on the loss of the anterior rather than on that of the posterior lobe. Paulesco's results have been confirmed in the main by Reford and Cushing (209), Crowe, Cushing and Homans (39, 40) and Goetsch, Cushing, and Jacobson (106) (*see also* Cushing, 43). These observers find that puppies survive total extirpation longer than do adults; that life can be prolonged (*see* Section E.) by transplantation of the removed gland; that, in all cases which recovered, a fragment of the anterior lobe was invariably found to have survived; that animals with a fragment of anterior lobe, temporarily insufficient to support life, could be tided over a period of threatened

cachexia hypophyseopriva by subcutaneous injections, or by feeding with anterior lobe ; and that removal of the posterior lobe leads to no very definite symptoms.

The acute symptoms observed were tremors, fibrillary twitching, arching of the back, insensitiveness, slow pulse and respiration, a terminal abrupt fall in body temperature, and apathy passing into coma and death.

Cushing and his collaborators describe in animals, which recover after partial extirpation, certain constitutional disturbances, some of which (*e.g.*, of carbohydrate tolerance) they now admit to be due in part to posterior lobe deficiency. These constitutional disturbances are adiposity, changes in the skin, disturbances of carbohydrate metabolism, of temperature, of growth, and of secretion by the kidney. Sexual inactivity and changes in most of the ductless glands are described too.

In some cases, the adiposity was so extreme that the weight of the animals became doubled, the deposition of fat is widely distributed, and in some regions œdema is recorded.

The skin becomes dense, dry, and less movable than usual. The hair becomes bristly and tends to fall out in patches—changes, as pointed out by Cushing, not unlike those found after thyroid extirpation.

When much pituitary substance has been removed, a subnormal temperature is the rule, and it may fall nearly to room temperature. The normal temperature may be restored by applying heat, but this hastens the end. In some cases, Cushing found, when the temperature was not very low, that it could be raised by ingestion, or subcutaneous injection, of pituitary extract. He states that a thermic reaction occurs, upon the injection of pars anterior preparations, only in cases of anterior lobe deficiency, and can be used as a clinical test when anterior lobe deficiency is suspected.

Pulse rate and respiration may be slow, and the blood-pressure low.

In young animals, partial pituitary extirpation results in disturbances of growth, especially in skeletal undergrowth.

Cushing also reports mental dulness, irritability, and a tendency towards epileptic fits.

After extirpation, a temporary glycosuria usually ensues,

followed by a short period during which the assimilation limit is below normal. Subsequently, the animals acquire such a tolerance for sugar, that it is often difficult to produce alimentary glycosuria with the amounts of sugar that can be retained. According to Cushing's observations, these facts are connected with removal of, or damage to, the posterior lobe, and the interpretation given by this writer is as follows : "Normal posterior lobe activity is essential to effective carbo-hydrate metabolism ; an intravenous injection of posterior lobe extract produces glycogenolysis, and its continued administration in excessive amounts leads to emaciation. A diminution of posterior lobe secretion occurring in certain conditions of hypo-pituitarism (whether experimentally produced or the result of disease) leads to an acquired high tolerance for sugars, with the resultant accumulation of fat."

It is reported that, contrary to what might have been expected, removal of the posterior lobe increases the flow of urine rather than diminishes it. There is often a true diabetes insipidus, lasting for some time.

Experiments upon puppies disclose a persistence of sexual infantilism. There are as well changes in the testes, ovaries, thyroid, thymus and adrenal cortex and medulla. Moreover, changes occur in the reverse direction, for example in the pituitary after castration or thyroidectomy, and Cushing reports changes in the posterior lobe after extirpation of the pancreas.

So far as can be gathered from Cushing's account (43), this author attributes most of the disturbances above described to deficiency of the anterior lobe ; indeed the only changes, which he definitely attributes to damage to the posterior lobe, are the effects upon carbo-hydrate tolerance and upon the secretion by the kidney. He does not state definitely whether these changes are due to loss of the nervous portion proper, or to that reflection of the pars intermedia which passes over the nervous portion.

Hanselmann and Horsley (115) have failed to confirm the results of Cushing and his colleagues. In their experiments there was a very high death-rate from shock, hæmorrhage, and infection ; but in the animals which survived, there were no characteristic symptoms like those described by Cushing.

Hanselmann and Horsley further state that they observed a parallel death-rate in animals, in whom incomplete extirpation had been carried out. It is clear that the results of this series of experiments are quite different from those obtained by Paulesco and Cushing.

Aschner (4, 5, 6, 7) has opposed the view that the pituitary body is essential to life. He operates through the roof of the mouth. In adult animals, according to Aschner, there are no serious symptoms after the complete operation, although there are slight metabolic changes. In young animals, on the contrary, profound effects are produced. In these cases, the symptoms described are analogous to those given by Cushing, and which are detailed above. His operative proceedings are criticised by Biedl[1] and by Cushing.

Quite recently, Aschner has emphasized the relationships between the pituitary body and the genital organs, and points out the bearing of these upon pathological conditions in the human subject.

Staderini (240) believes that extirpation experiments have given contradictory results in the hands of different observers, because operators have not always taken account of the "lobi laterales" and the "lobus premamillaris," described by him in the cat and in the ox (238, 239). Perna (205) has given a full description, with illustrations, of a "post-glandular prolongation" in the human subject. Other "accessory pituitaries," which may be mentioned here, are the "pharyngeal pituitary bodies" described by Haberfeld (108), Erdheim (79, 80), Novi (186), Arena (3) and Pende (204).

Complete extirpation can never be said to have been performed, unless these accessory bodies have been removed along with the main pituitary. Moreover, according to Biedl, total extirpation can only be described as such when, in addition to the removal of both lobes, the hypophyseal peduncle is severed as well. This latter operation is in itself, according to Biedl, as fatal as complete extirpation of the pituitary body. This was found to be the case also by Paulesco, and Aschner has only recorded the survival of animals in pituitary operations when not too much of the infundibulum was removed. Morawski (183), however, found that cutting through the

[1] "Innere Sekretion, etc." 2te. Aufl., 1913, Berlin u. Wien.

peduncle has no serious effect on the monkey, while cats will not survive the procedure. This difference is explained by him by the fact that, in the monkey, cutting through the peduncle does not make an opening into the third ventricle, which must happen in cats and dogs. Biedl thinks that the real explanation lies in the anatomical relationships of the pars intermedia in the different animals, and is of the opinion that the opening of a communication with the third ventricle is a matter of no consequence.[1]

Summing up, so far as is possible, these somewhat contradictory experimental results, we may conclude with some degree of probability that :—

1. Total extirpation of the pituitary body is a fatal operation, though the duration of life in the operated animal varies very considerably according to its age. Adult dogs and cats will not survive more than two or three days ; young animals may live as many weeks.

2. Partial extirpation of the pituitary body (if a small part of the anterior lobe be left behind) gives rise to disturbances in growth and metabolism already described, and these may be induced in young animals by deficiency of anterior lobe only.

3. The effects upon the genital organs may be due to deficiency of the pars intermedia, and the preponderance of evidence is that the polyuria and disturbance of carbohydrate metabolism (tolerance) are due to deficiency of this part as well.

4. It seems possible that removal of the nervous portion proper would be without any serious effects. This operation can, however, scarcely be carried out without damage to the pars intermedia, and this damage brings with it the metabolic disturbances just referred to.

It is interesting to note that, just as in the case of the adrenal body, so we have in the pituitary two main portions, one of them glandular, the other nervous. In the case of both organs, the physiologically active substances are found in the nervous portion (neurohypophysis, adrenal chromaphil tissue), while the glandular portion seems to be that which is

[1] Edinger (71) has recently offered still another explanation.

essential to life.[1]

H.—THE QUESTION AS TO A FUNCTIONAL RELATIONSHIP BETWEEN THE PITUITARY AND THE THYROID BODIES.

From the time when the ductless glands first began to be known, there has been a decided tendency to regard them as physiologically more or less related to one another. In the earliest days, there can be little doubt that the grouping together of these organs was very largely to be ascribed to our uniform ignorance of their functions. But during recent years a certain amount of information has been accumulated, which renders it probable that there are true inter-relationships between certain of the glands endowed with the power of internal secretion. The whole question constitutes, or will constitute, a very fascinating, albeit a very abstruse, chapter in the physiology of internal secretion. We are, however, in this place concerned only with a possible functional relationship between the thyroid and pituitary bodies.

Many of the suggestions which have been made were of an *à priori* character. Cyon (46, 60) has put forward a theory of an elaborate kind about the mutual function of the thyroid and pituitary bodies, and he regards the latter as a centre from which the vascular supply of the brain is influenced through the former. Sajous (215) apparently postulates a relationship between the various ductless glands, whose functions, according to this writer, dominate most of the bodily activities, normal and pathological.

Rogowitsch (212), in 1888, observed in rabbits, killed at periods of from two to ten weeks after thyroidectomy, a marked hypertrophy of the pituitary body. This result was confirmed by Hofmeister (123), Stieda (242), Gley (105), Pisenti and Viola (207, 208). Schönemann (231), Torri (249), Herring (120), Lucien and Parisot (170), Parhon and Goldstein (198), Leonhardt (151), and Traina (250) found only a moderate degree

[1] In making this analogy the pars intermedia is treated as if it were a part of the posterior lobe. Quite recently Ascoli and Legnani (9, 10) have re-investigated the effects of extirpation of the pituitary body. They confirm in the main the views put forward above and add several important facts concerning changes in the other internally secreting organs.

of hypertrophy.

Quite recently Lydia M. Degener (64) has found that the increase in weight of the pituitary, after the thyroid glands have been "completely removed"[1] from rabbits, runs parallel with the time which intervenes between thyroidectomy and the death of the animal. After an interval of 179 days, the pituitary body had increased to about three times the normal size.

In these hypertrophied pituitaries there is increased activity of the cells of the pars intermedia, and in the proper nervous part of the posterior lobe. In these situations, granular, hyaline, or colloid bodies become very numerous; they appear to be partly of a cellular nature and to find their way between the ependyma cells into the infundibular recess and ventricles of the brain. The colloid appears to arise from the epithelial cells of the pars intermedia.

Viguier (254) reports that in a lizard he has found some temporary modification of the pituitary after thyroidectomy. It further appears[2] that removal of the parathyroids produces in the pituitary body compensatory changes similar to those induced by the removal of the thyroid.

The precise nature of the relationship existing between the thyroid apparatus and the pituitary body is by no means clear. Cimorini (28, 29) cannot find any changes in the pituitary after parathyroidectomy. Simpson and Hunter (236, 237) report that complete removal of the thyroid gland in lambs does not lead to the appearance of iodine in the pituitary. On the assumption that the iodine containing substance of the thyroid represents its active secretion, this does not support the Rogowitsch theory that, in thyroid insufficiency, the pituitary vicariously takes on its function. In the experiments of Simpson and Hunter, there was, however, some compensatory hypertrophy of the pituitary body.

It only remains to make reference to some experiments of Masay (178) in opotherapy, with the object of ascertaining whether pituitary extract can replace the internal secretion of

[1] This means, presumably, that the thyroid and internal parathyroid on both sides were removed, leaving behind both external parathyroids.

[2] F. D. Thompson, *Phil. Trans.*, 1910.

the thyroid; the results were entirely negative.[1]

I.—PITUITARY INSUFFICIENCY AND A PITUITARY ANTISERUM OR CYTOTOXIN.

Masay (178) has attempted to produce pituitary insufficiency by the method employed by Demoor and Van Lint (68), in order to obtain an "anti-thyroid serum." Guinea-pigs were injected intraperitoneally with an emulsion of dog's pituitary at intervals of two days. After three, four, or five injections the blood of the guinea-pig was collected and centrifugalized, and the serum (about 10 c.c.) was injected under the skin of a dog. Masay gives his results in considerable detail, and the effects upon the animal are shown in a series of illustrations. After a certain number, usually two or three, of such injections the dogs show symptoms, such as loss of flesh, muscular weakness, especially in the hind limbs, changes in the skeleton and in the structure of the pituitary, the symptoms constituting, according to Masay, a veritable cachexia hypophyseopriva.

Ossokin (192) reports that the "hypophyseolytic serum," prepared from the blood of dogs immunized with posterior lobe of pituitary, produces a marked fall of blood-pressure. The precise significance of this is difficult to understand.

It is yet too early for us to be able to determine the value of these antiserum experiments.[2]

J.—CHEMISTRY OF THE PITUITARY BODY.

Schäfer and Vincent (226, 227), who described a pressor and a depressor substance, found that the latter could be separated from the former, on account of the fact that it is soluble in alcohol, in ether, and in normal saline solution. It has since been shown, by the present writer and collaborators, that this depressor substance is common to all animal tissues.

Schäfer and Herring (224) contend that two active principles exist in pituitary extracts, one acting on the circulatory system, the other specifically on the kidney. Dale (62) does not consider the evidence on this point to be satisfactory.

Within recent years two observers have claimed to have

[1] For a general discussion of the relations between the pituitary and the other ductless glands, *see* F. Duncan (70).

[2] On this subject, *see* Parisot (200).

obtained, apparently independently, the active substance in a pure form. Houssay (133) in 1911 prepared the active substance as follows :—"The fresh hind lobes were boiled in water ; the filtrate was then precipitated with lead acetate and sulphuric acid, filtered, and the filtrate dried *in vacuo*. The residue is washed with chloroform, ether, and alcohol, and finally crystallized *in vacuo*. The product is insoluble in alcohol, ether, or chloroform, but very soluble in water, and is dialysable. It is precipitated by picric acid, platinum chloride, etc. If burnt on platinum foil, it gives off the smell of burnt feathers."

Solutions of this product in normal saline produce the effects of pituitary extracts upon the heart and vessels.

Fühner (97, 98) claims as well to have isolated a pure crystalline basic substance, which has been put upon the market in the form of its sulphate, and is called *hypophysin*. Fühner's product possesses all the activities of pituitary extracts on respiration, blood-pressure, and the uterus.

Herzberg (122) has tested Fühner's substance clinically, and reports that its action upon the uterus is powerful and prompt. "Hypophysin" is stated to consist of four separate substances.

In still later papers, Fühner (96) and Schickele (228) declare that the substance acting upon the uterus is independent of that acting upon the blood-pressure, and can be obtained from extracts of the anterior as well as of the posterior lobe.[1]

K.—SUMMARY.

1. The pituitary body consists of three parts : (*a*) anterior lobe or glandular portion ; (*b*) intermediate portion ; (*c*) posterior lobe or nervous portion.

2. It seems to be well established that the pituitary body is an organ essential for life, and that the part which is so essential is the anterior lobe or glandular portion.

3. The anterior lobe is related in some way to the growth of the body, especially of the skeleton, and there seems to be a correlation between the pituitary body and the sexual organs, since, after experimental operations, or in disease, in

[1] Kraus (150) deals with the lipoids of the human pituitary, and Butow (21 finds several ferments present in the organ.

growing animals, there is a condition of sexual infantilism.

Important changes occur in the anterior lobe during pregnancy. The chromophobe cells (*see* Section A.) show changes in the nucleus and in the protoplasm, and become markedly eosinophile; they are now referred to as pregnancy cells (Erdheim and Stumme, 81; Siguret, 232).

4. The intermediate portion secretes one or more hormones, which have the power of raising the blood-pressure, slowing the heart-beat, increasing the activity of smooth muscle, and causing increased secretion of the urine, the gastric juice, and the milk.

5. The active principle or principles, just referred to, can be obtained in greater amount or in more concentrated form in the nervous portion proper. This indicates that the secretion takes place in the pars intermedia, and that the substances secreted are passed on into the nervous portion proper, where they become converted into more active forms, or become concentrated.

6. The pars intermedia probably exercises some kind of control over carbohydrate metabolism.

7. It is believed by many authors that the hormone or hormones secreted by the pars intermedia are contained in certain hyaline bodies, which are pushed through the neuroglia of the pars nervosa into the third ventricle of the brain, and that they may be found subsequently in the cerebro-spinal fluid, and thus, in a roundabout manner, they find their way into the circulation.[1]

7. There appears to be good evidence for the existence of some kind of relationship between several of the organs known as ductless glands. That there is some connection between the pituitary body and the thyroid is shown by hypertrophy of the pituitary, and an increase in the colloid vesicles of the pars intermedia after extirpation of the thyroid.

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[1] Carlson and Martin (22) state that the cerebro-spinal fluid of the dog, when injected into a dog, does not raise the blood-pressure, nor has it any effect on the carbo-hydrate metabolism; in spite of this, the authors think it is possible that a certain amount of pituitary secretion is present in the cerebro-spinal fluid. (*See also* Wassing, 259.)

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Special Number on the Internal Secretions—Part II.

THE THEORY OF THE INTERNAL SECRETIONS.

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One of our most distinguished surgeons, Professor W. S. Halsted,[1] of Johns Hopkins University, wrote recently: "It must be evident to everyone that there reigns the greatest confusion on the subject of the functions of the glands of internal secretion." It is obviously difficult, under these conditions, to comply with the request of the Controlling Editor of The Practitioner to prepare an article on the above subject. To do it at all, in fact, necessitated the avoidance of what appears to have been the underlying cause of the confusion referred to, which is the prevailing custom of elaborating conclusions and even theories on data too few to warrant them.

It has always seemed to me that it was only through the resources of analytic and synthetic reasoning on broad lines, *i.e.*, on the basis of data, contributed by a large number of competent investigators in every branch of normal and morbid biological science, concerning the ductless glands, that we could hope to obtain at least an approximate idea of the functions of these organs. Such a comprehensive survey of available data formed the basis of a work, the first edition of which was submitted many years ago.[2] What influence this work has had upon the development of the question as it stands to-day is difficult to say, but the facts remain that many of the deductions submitted in its pages have been sustained directly or indirectly by subsequent experimentation, and that the trend of modern thought seems suggestively to follow the clues it tentatively indicated at the time. It is because of this that the plan then followed will be adhered to in the present

article, the salient features being alone introduced to avoid abuse of space.

THYMUS.

The thymus is considered first owing to its temporary character as regards functional activity; this, as is well known, usually lasts up to adolescence, the organ having by that time become gradually replaced by adipose tissue. Hence arises its early association with development. Analysed, this assumption gains support in all directions. In status thymolymphaticus, growth, particularly that of the bones, is stunted; there is defective development of the genitalia, including that of pubic hair, and low resistance to disease, particularly infections and intoxications. Removal of the organ does not directly compromise life, but it impairs strikingly the development of the osseous system; a rickets-like condition results; the bones become soft and pliable, sufficiently so in some instances to result in genu varum; they are more readily fractured, owing to slow calcification. This is due to a reduction of the calcium in bones and other tissues (Bracci, 1905), a fact accounted for by the high excretion of this element in thymectomized animals (Basch), and sustained by the observation of Soli that thymectomized hens lay eggs without shells. The influence of the thymus on the osseous system is further shown by the fact that the implantation of thymus in thymectomized animals causes a resumption of growth, especially marked in the long bones (Sommer and Floecken, 1908). The nature of these morbid effects and of the *rôle* of calcium in the process points clearly to the identity of the underlying cause, viz., a defective formation of calcium phosphate.

Whence comes, however, the phosphorus required in the process? This recalls another feature of thymic chemistry; the wealth of the thymus in nucleinates, its lymphoid cells, according to Chittenden,[3] containing a nucleoproteid rich in phosphorus, 3·5 per cent. It becomes a question, however, whether this phosphorus enters at all into the physiological functions of the organ. That such is the case is shown in various ways. Thus, removal of the thymus in dogs is followed by clear evidences of idiocy (Morel, 1914).[4] At the request of Bourneville, Katz[5] performed autopsies in 61 mentally normal children, who had died of various diseases, varying in age from one

month to 13 years; in all of these the thymus was present. In 28 mentally weak children examined post-mortem by Bourneville, however, the thymus was absent. In another series of 292 cases of mentally deficient children, the organ was absent in 74 per cent. At Bicêtre, from 1890 to 1903, autopsies of 408 non-myxœdematous idiots ranging in age mostly from 1 to 5 years—none being above 15 years—showed the thymus to be present in only 104 instances (Morel, 1914). Lange and Dicker, Garrè and Lampé have reported cases of idiocy, in which at autopsy the thyroid was found quite normal, while the thymus was very small. That phosphorus is a fundamental constituent of cerebral tissue need hardly be emphasized.

Yet the bones and central nervous system are not the only structures morbidly influenced. Ruhräh[6] has reported 18 cases of infantile marasmus, in which the thymus alone showed lesions. Notable atrophy of the organ was also found in 20 cases of marasmus in infants, under 1 year old, by R. L. Thompson.[7] Dudgeon[8] was led to conclude that atrophy of the thymus was the most characteristic feature of marasmus. Rohrer, Bovaird, Nicholl, Warthin, Rachford, and others have defended the same view. When we recall the influence of thymectomy on the organism at large, and the general trophic disturbances and defective development this operation entails, we cannot but be impressed with the declaration of Friedlieben as far back as 1858, that "the size and condition of the thymus is an index to the state of nutrition of the body." The influence of the nucleins, or at least of the phosphorus in the nucleinates, which the lymph cells of the thymus contain is thus not exercised over a particular tissue but over all tissues.

How is the phosphorus transmitted from the thymus to the tissues? This question finds an answer in the relationship between persistent thymus and Graves's disease. In 133 cases of the latter disease, in which death had followed operation, Mattis found, for instance, that 76·5 per cent. had an abnormally large thymus. The labours of Klose, Capelle, and others have so distinctly shown that a persistent thymus could produce Graves's disease, that thymectomy, first found efficient by Garrè, is regarded as a warranted procedure. Now, this operation confirms what experimental medicine had demons-

trated, viz., that thymectomy caused a gradual decrease in the leucocyte count, while the administration of thymus caused an increase of these cells. In Graves's disease due to persistent thymus, the operation not only reduces the tachycardia, but also a typical symptom to which Kocher called attention, lymphocytosis. In Garré's case, removal of the thymus brought the lymphocytosis down from 40 to 10 per cent.; other surgeons, including Halsted (1914), have observed the same phenomenon. This shows plainly that the thymus is the source of the excess of lymphocytes in the blood—a fact which in itself points to the mode of distribution of the nucleins, or phosphorus in organic combination, since we have seen that thymic cells are rich in nucleinates.

These few facts appear to me to indicate the drift of our knowledge towards a possible function of the thymus gland. At least the following theory (the same, in its general lines, that I submitted years ago, before many of the confirmatory data adduced had been recorded) may be said to encompass the greatest number of scientific facts :—

The function of the thymus is to supply, through the agency of its lymphocytes, the excess of phosphorus in organic combination, or nucleins, which the body, particularly the osseous and nervous systems, requires during its development and growth.

Additional testimony is afforded by the fact that this theory supplies a solid foundation for the various thymic syndromes. Thus, it accounts for thymic idiocy through deficiency of phosphorus in, among others, the central nerve cells; for thymic Graves's disease, through the toxemia induced by an excess of nucleins, or possibly, nucleic acid; for thymic marasmus, through deficiency of cellular nucleins in all tissues; and finally, for thymic dwarfism and rachitis through deficient formation of calcium phosphate.

If we now try to explain these syndromes by the theories that have been advanced by as many investigators—all based on a restricted survey of their experimental results—it will be found impossible to do so. They are as follows :—That the thymus gland is the mother tissue of all lymphoid structures; that it fits out the leucocytes for their various functions; that it is in some sort of relationship with the reproductive glands; that its internal secretion is an antecedent of that supplied by

the reproductive organs when fully developed; that it prevents the excessive accumulation of acid in the body, phosphoric acid in particular; that it has an action antagonistic to that of the adrenals and thyroid. Each of these conclusions fits more or less accurately a set of isolated observations; but none provides the comprehensive grasp that a *bonâ fide* function of an organ should possess.

PANCREAS.

As first pointed out by Lépine in 1889, the pancreas is the source of an internal secretion which he termed glycolytic ferment. Its presence is shown by the fact that ligation of Wirsung's duct, which should provoke glycosuria, as does complete removal of the organ, fails to do so. It is produced, in the light of prevailing views, by the *sui generis*, and constantly reformed, islets of Langerhans which, as first shown by Schäfer, sustain carbo-hydrate metabolism. When the functions of these islets are inhibited through local atrophy, hyaline degeneration, sclerosis, etc., whether the rest of the organ be involved or not, diabetes appears. Conversely, Opie, MacCallum and others, have shown that, if the islets are intact, *i.e.*, uninjured, glycosuria will not occur.

The glycolytic action of the product of the islets *in vitro* was shown by Diamare and others to be such as to require the intervention of some other agents or secretion. I suggested (1907),[9] after a close analysis of the question, initiated by Blum's work, that the adrenal secretion—which I regard as Pawlow's "ferment of ferments"—was the main factor in the process. W. G. MacCallum (1911)[10] states that the weight of evidence is in favour of the idea that the adrenal secretion can "in some way stir up the tissue [of the islets] to set free sugar into the circulation or mobilize the carbohydrates." Eppinger, Falta, and Rudinger[11] hold that it does so by inhibiting the action of the pancreas, but this is denied by MacCallum and others. From my view-point the inhibition referred to by Eppinger, Falta, and Rudinger is due to excessive experimental dosage. Hoskins,[12] for instance, states, referring to the adrenal secretion:—"This secretion acts strongly in remarkably dilute solution. For instance, the presence of 1 gm. in 100,000 litres or 1 grain in 1,500 gallons of fluid

bathing a piece of isolated intestine is sufficient to check its activity." Now, when we consider that the chief effect noted by Oliver and Schäfer was contraction of the arterioles, it is obvious that the dosage used by Eppinger, Falta, and Rudinger sufficiently constricted the pancreatic arterioles to diminish greatly the arterial blood supplied to the organ, and thus inhibit its functions, including that of the islets of Langerhans. Benedicenti, Glässner, and Pick, for instance, found that it took large doses of adrenalin to inhibit the secretion of the pancreas. The functions of the adrenals, to be described later, will suggest the process through which their secretion activates that of the islets.

On the whole, the prevailing opinion, based on sound evidence, is that *the pancreas produces an internal secretion which governs carbohydrate metabolism in the organism at large.*

The second function in which a pancreatic secretion takes part is one to which I first called attention in 1903, and which Abderhalden has independently confirmed in many particulars by brilliant researches begun in 1905.

We have just seen that the internal secretion of the pancreas governs carbohydrate metabolism. According to Abderhalden[13] it is "quite certain that the cells of the body are capable of hydrolytically splitting fats into alcohol and fatty acids. Further, they are able to decompose carbohydrates of a complicated structure, especially glycogen, through dextrines and maltoses." The actual source of these ferments is not established, but in the light of the foregoing facts it is reasonable to assume that it is the pancreatic internal secretion. Again, Abderhalden states that "everything points to the fact that the cell has agents at its disposal which render it capable of splitting up into their simplest units all the complicated substances which are brought to it or which it itself builds up." In other words, "each separate cell, with very few exceptions, disposes of the same or similar ferments as those secreted by the digestive glands in the intestinal canal." As these agents include lipase, amylopsin, and trypsin, all pancreatic ferments, we are again brought to the pancreas as the source of the cellular ferments in the body at large.

As to the manner in which these ferments are conveyed to the tissue cells, Abderhalden writes: "It is an open

question from what source these ferments, which we are going to call defensive ferments, take their origin. Many facts accord with the suggestion that the leucocytes play a part in this connection. They probably give off these ferments to the circulation." He gives as examples the demonstrable ferments in the pulmonary alveoli, which ferments "take their origin from leucocytes"; the migration of multitudes of leucocytes to oppose an invasion of micro-organisms, etc. He holds, therefore, that "the old view whereby leucocytes take up substances from the outside and digest them, must now be completed by the observation that ferments can be given off to the exterior, and that, therefore, digestion may be accomplished outside the cell."

While very dissimilar cells of the body may thus contain various ferments, the purpose of the latter, according to Abderhalden, is to decompose albumen into peptones. It can "be easily shown," he writes, "that the cells of the body are able to decompose into their structural units the so-called polypeptides, that is amino-acids linked in the manner of acid amides. These ferments have acquired the name of peptolytic ferments. Their presence has been demonstrated in animals and plants in the most varied kinds of cells." It is further asserted that "each separate cell of the body is capable of digestion," this applying only to ingested foods of a structure harmonious with the structure of the cell. Such materials are alone, through the intermediary of the liver and lymphatic system, permitted to reach the cell. We thus have digestive ferments as active participants in the metabolism of tissue cells.

Abderhalden terms "defensive ferment" the agent, or aggregate of agents, which is able to deprive of their specific character disharmonious, *i.e.*, more or less toxic, agents of endogenous or exogenous origin, the object being "to bring the so-called reactions of immunity into close line with processes that are normal and consequently familiar to the cells." On the principle that under normal conditions substances which are toxic, *i.e.*, out of harmony with the plasma, never have access to the blood, it seems apparent that the blood plasma should be normally lacking in digestive powers. This proved experimentally to be true; the blood plasma has

never been found "either in the majority of animals or in man to produce decomposition of albumen, peptones or polypeptides." Yet after a meal rich in fat, active lipase could be demonstrated in the blood, while after the introduction parenterally of nucleoproteids, nuclein, and nucleic acids, ferments appeared in the blood plasma in increased quantity and quickly reduced these substances. This applied as well to cane sugar as determined in the dog by the optical method.

As to pathogenic germs and their toxins, the gastro-intestinal tract and the liver afford the first line of defence for ingested organisms, while the lymphatic system "watches that no material shall reach the blood which is out of harmony with it" whether of endogenous or exogenous origin. When, however, the actual invasion of organisms occurs "the harmoniously organized cells of the tissues are subjected to the influence of a kind of cell which has an utterly strange organization of its own." Each cell of the body, with very few exceptions, has been found to dispose of ferments similar approximately to those secreted by the digestive glands; here, as in the blood, the pathogenic organism and its products are subjected to the action of defensive ferments.

That the tissue cells themselves are not disintegrated by these ferments is provided against, according to Abderhalden, "by giving them a structure and configuration . . . which are out of harmony with the ferments." Be this as it may, the fact remains that in the light of his experimental work, Abderhalden attributes to ubiquitous digestive ferments not only an active *rôle* in cellular metabolism of the body at large, but also defensive properties.

The process which I had previously described [14] was based mainly on a study of the trophocytes of sponges, personal laboratory study of the properties of ferments in lower forms, and a comprehensive search into the literature on the subject of nutrition by white corpuscles. It introduced, as main proteolytic agent in both tissue metabolism and the defence of the body against infection and intoxication, a trypsin-like ferment, and differed only from Abderhalden's independent conclusions in that the granulations of *certain* leucocytes supplied their end products of food stuffs to the tissue cells

for their upbuilding, besides the digestive ferments referred to.

I summarized, at the time, the prevailing views concerning the presence of ferments in leucocytes, in the following words: "The presence of trypsin and other ferments in leucocytes is now recognized as a fundamental feature of phagocytosis. Metchnikoff's cytase is regarded by him, and by Bordet and others, as a trypsin; Kanthack and Hardy also attribute the proteolytic activity of leucocytes to soluble ferments. The more recent writers refer increasingly to the presence in leucocytes of such a ferment." . . . "That trypsin is the bactericidal agent of the intestinal tract has been shown by Charrin and Levaditi, Zaremba and others." M. Labbé says, after referring to the oxidase fibrin ferment, etc., found in these cells: "They contain, moreover, a *fibrinolytic* ferment (Leber, Achalme), a *casein* ferment, a ferment analogous to *trypsin*, a *glycolytic* ferment (Rossbach, Zabolotny, Tarchetti), a *lipasic* ferment which, as shown by Poulain, plays an important *rôle* in the assimilation of fats—briefly all the hydrolytic ferments of the pancreatic juice."

After showing that the leucocytes may be traced from the intestinal walls laden with peptones, that they shed their granulations through canaliculi, both in the blood and in the tissue cells, and indicating the *rôle* of oxidation in the process, etc., I submitted, among other conclusions, that the products of gastro-intestinal digestion "are taken up from the intestinal canal by leucocytes, the digestive leucocytes, which then enter the circulation; and that after terminating the digestion of peptones ingested by them, the leucocytes convert the end products into granulations, *i.e.*, into a compound suitable for assimilation by the cells of the body at large." The leucocytic proteolytic ferment plays a dual *rôle* from my view-point; it completes the digestion of the peptones which their host, the leucocyte, carries from the intestinal canal to the tissues, and in the latter serves to carry on the katabolic phase of the metabolic process.

In the blood, the same leucocytes carry on their share of the defensive process, as I interpret it, by secreting their digestive ferments in the plasma when needed, *i.e.*, when it is invaded by bacteria, toxins, toxic waste products, or other substances harmful to the tissue cells. The katabolic phase

of metabolism here serves to break down the pathogenic substances, endogenous or exogenous, precisely as it does worn-out components of the tissue cell. As we shall see, however, this defensive process requires, as does cellular metabolism —as I understood both these functions already in 1903—the intervention of other agents—products, as will be shown, of ductless glands other than the pancreas.

In the light of the foregoing, and particularly of the experimental confirmation of the bulk of my views by Abderhalden, it seems permissible to conclude that *besides governing carbohydrate metabolism, the pancreas supplies ferments which take a direct part in the protein metabolism of tissue cells, and also in the defensive reactions in these cells and in the blood stream.*

ADRENALS.

In his review (1913) of the voluminous literature on these organs, Swale Vincent writes,[15] "It is regrettable to have to admit that we are still unable to give a full and satisfactory answer to the question, What is the function of these bodies?" Confusion has arisen, it seems to me, mainly through the many directions in which the secretion of the adrenals has shown activity. It helps to maintain the tone of muscles, especially those supplied by the sympathetic; it raises the blood-pressure, and increases the power of the heart while slowing its beats; it enhances carbohydrate metabolism; it destroys toxic wastes of muscular origin; it reduces fatigue. Again, the fact that its supply is increased by fear, pain, strong emotions and asphyxia suggests some compensative action to counteract the wear and tear produced by these conditions. These, obviously, are not functions, but merely segmental expressions of a *general* function. The identity of what I thought the latter to be I pointed out eleven years ago. As will be shown, it accounts for all the properties just described.

The process through which the body is supplied with oxygen is still obscure. The absorption of oxygen by the pulmonary blood persists even when the pressure of this gas is almost *nil*. A strangulated animal exhausts the air in its lungs of *all* its oxygen, while only traces of oxygen are to be found in the arterial blood of asphyxiated animals.[16] These facts have long emphasized the belief that the diffusion doctrine

was defective, and that the absorption of oxygen from the air was due to the presence, in the blood circulating through the lungs, of some substance capable of taking up this gas. This conclusion was sustained by the researches of Bohr and others, Bohr and Henriques concluding that the substance "having greater avidity for oxygen than the blood itself" in the lungs was presumably "a kind of internal secretion."[17]

The advocates of the diffusion theory (whose aerotonometric figures are suggestively discordant) have opposed this view, but, as stated by Pembrey, "the body of evidence has been steadily increasing in favour of the secretory theory, especially as regards the absorption of oxygen."[18]

Adrenal extractives being endowed, as is well known, with marked reducing properties, it appeared to me eminently fitted to act as the "internal secretion" sought by Bohr. Anatomical studies in lower animals and in man, and a systematic research in the literature of the subject showed that this assumption was sustained by a large number of experimental and clinical facts, the principal of which were as follows :—

1. The secretion of the adrenals, while possessing a marked affinity for oxygen, inevitably reaches the pulmonary air-cells. The blood of the efferent vessels of the adrenals, their veins, passes to the inferior vena cava, directly on the right side, and by way of the renal vein on the left. The actual presence of the adrenal secretion in the blood of the adrenal veins is shown by many experimental facts. Hyaline granules (found subsequently to be their secretion) passed from the interior of the adrenals to their veins.[19] The same granules were traced from the interior of the organ along the adrenal veins to the vena cava itself.[20] It is doubtless the adrenal secretion, and no other, which is carried by the blood of the vena cava ; for, when blood originating from the adrenals on its way to this great trunk was injected into animals, it produced the characteristic effects of adrenal extract, while such effects could not be obtained with venous blood obtained from other parts of the body.[21] In the lungs the adrenal principle dilates the bronchioles, obviously to aid respiration and to increase the air intake.[22]

2. On reaching the air cells, the adrenal secretion absorbs

oxygen, and becomes a constituent of hæmoglobin and of the red corpuscles.

Gamgee states that "hæmoglobin exists in the blood corpuscles in the form of a compound with a yet *unknown constituent* of the corpuscles." This body he defines as the "albuminous moiety of the hæmoglobin molecule" and as representing 96 per cent. of this molecule, the remaining 4 per cent. being the iron-laden hæmatin. Now this "unknown constituent" of hæmoglobin corresponds in its physicochemical properties with the adrenal secretion.[23] Thus, hæmoglobin is insoluble in absolute alcohol, chloroform, benzol, ether, and all organic solvents; of all glandular products, that of the adrenals alone shows this peculiarity.[24]

Again, adrenal extracts are rapidly destroyed by alkalies; this is also a characteristic of hæmoglobin.[25] This pigment likewise resists heat up to the boiling point; this applies also to adrenal extract.[26] Moreover, Mulon found that the red corpuscles gave the histochemical reactions of the active principles of the adrenals, thus showing that these blood cells actually contain this principle.[27] Bröking and Trendelenburg [28] found adrenalin in normal blood in the proportion of about 1 to 2,500,000 and that this proportion was doubled and sometimes quadrupled in true exophthalmic goitre. J. L. Miller [29] found it increased four or five times in simple goitre. Batelli [30] isolated from the blood a product endowed with the chemical properties of adrenalin. This adrenal principle is, doubtless, present in the albuminous portion of hæmoglobin voided by red corpuscles into the plasma; for the latter contains an oxidizing substance or oxidase (the adrenal ferment dealing out the oxygen it took up in the lungs) which resists heat to the boiling point, and possesses other chemical characteristics of the adrenal principle.[31] Again, while in 1853 Traube had concluded that hæmoglobin could not fulfil the physiochemical functions ascribed to it without the aid of a catalyser, Poehl [32] showed that the adrenal principle was a catalyser, and Jolles [33] found that the activity of a given volume of blood as a catalyser corresponded with the number of red corpuscles it contained.

3. The red corpuscles, after absorbing the oxygenized adrenal secretion (the albuminous constituent of their hæmo-

globin) yield it to the blood plasma in the form of droplets.

Louis Elsberg,[34] many years ago, observed "a projection of a pediculated granule or knob" from the periphery of red corpuscles. Hirschfeld[35] traced these granules from the interior of these cells through one or more minute apertures, which closed up again, to the surrounding plasma. Brockbank[36] gave recently a beautiful microphotograph of "platelets in, or being extruded from red cells." Again, Detemann[37] noted that the buds on the surface of the red cells "at first are attached to the cell by protoplasmic processes and contain hæmoglobin"; but that "later, the buds become separated fromt he cell, losing their hæmoglobin." The colouring matter remains in the corpuscles, the albuminous constituent being alone voided into the plasma.

Biedl[38] states that "the entire question of pigmentation in Addison's disease is urgently in need of further investigation." The following data have seemed to me to indicate that:—

4. The albuminous constituent of the hæmoglobin, or oxygen-laden adrenal secretion, is distributed by the red corpuscles to all parts of the body as an oxidizing agent.

Most classic writers consider melanins, the brown and black pigments found, in certain forms of sarcoma, in the tissues, the blood, the urine, etc., in various morbid states, as hæmoglobin derivatives.[39] While Mörner, Brandl, and L. Pfeiffer[40] found that it contained iron, and accept this origin, Nencki and Berdez[41] do not, because they failed to find this metal in the pigment isolated from a melanotic sarcoma. These discordant opinions are harmonized, however, by the newer conception I submit. The first-named authors dealt with whole hæmoglobin, containing, therefore, its iron; while Nencki and Berdez dealt quite as surely with hæmoglobin, but only with its albuminous constituent.

Having traced to the adrenals the origin of the active agent of this albuminous hæmoglobin, and this substance being melanin, the presence of the adrenal principle in melanins must be shown. In the first place, these pigments were found by Walter Jones[42] insoluble in alcohol, ether, benzol, chloroform, etc., *i.e.*, precisely as is the case with the adrenal principle. This applies as well to the action of alkalies, to which Jones, Abel, and Davis[43] found melanins

very sensitive, and to other tests. In the second place, direct evidence was afforded by Boinet,[44] who found, chemically, that the bronze pigment of Addison's disease was identical to melanin, and also by Mühlmann,[45] who discovered independently that the Addisonian pigment was a product of the adrenals. Its deposition as bronze pigment is due from my view-point to regional slowing of the capillary circulation.

A connection between the adrenal product and respiration and oxygenation is further sustained by the fact that (5) an excess of adrenal secretion causes a rise of temperature. This action was first observed by Oliver and Schäfer.[46] Reichert[47] recorded a rise of 1° C. in rabbits, accompanied by increased metabolism. Morel[48] noted a rise of 0·5° to 1° C. (0·9° to 1·8° F.) in guinea pigs. Lépine[49] states that the increase of blood-pressure caused by adrenal extract is always followed by a rise of temperature. This is controlled by the familiar fact, first observed by Brown-Séquard, that removal of the adrenals is followed by a steady decline of temperature, and also by the hypothermia which attends Addison's disease. Finally, Fuchs and Roth[50] found that subcutaneous injections of adrenalin (1·0 to 1·5 mg.) caused the respiratory rate to rise, while increasing the intake of oxygen and the output of carbon dioxide. This was confirmed by Bernstein and Falta.

As previously inferred, this is but a part of the evidence on this particular feature of the general problem. I studied, for example, the evolution of the red corpuscles throughout the animal scale,[51] and learned that they were tardy additions to the blood as storage cells, when the hæmoglobin diffused in the plasma, as it is in many invertebrates and in certain low vertebrates, failed to satisfy the needs of the vital process. Having been brought to the conclusion that, contrary to what is now taught, it is the plasmatic adrenoxidase or hæmoglobin which carries oxygen to the tissues and not the red cells, I traced this substance in various tissues and organs, including the nervous system (1903), the guaiacum and methylene blue tests being those most frequently employed. The oxidases having given the reactions of the oxygen-laden adrenal secretion, I applied to the latter the term, *adrenoxidase*.[52]

On the whole, the foregoing evidence seems to me to

have suggested that *it is the adrenal secretion which, after absorbing oxygen from the pulmonary air, and being taken up by the red corpuscles, supplies the whole organism, including the blood, with its oxygen.*

The adrenal secretion, thus considered as the active agent in sustaining general oxidation, explains the many properties attributed to that secretion enumerated at the beginning of this section :—As oxidizing agent, it influences the whole musculature, but particularly that supplied by the sympathetic system, because, as stated by Biedl,[83] "the neuro-muscular junction tissue [principally acted upon by adrenalin] is characteristic of the sympathetic system"; this, however, does not prevent an action on skeletal muscles, as shown by the experiments of Cannon and Nice.[84] The rise of blood-pressure is a result of increased oxidation in the cardio-vascular muscles. Its influence on carbohydrate metabolism is due to the fact that hastened oxidation enhances sugar hydrolysis in the tissues at large; whilst pancreatic glycosuria is due to the increased production of amylopsin, owing to increase of oxidation in the pancreas. The destruction of muscle and other wastes, including those due to fear, anger, etc., is due to its active participation in a defensive process in which, as we shall see, oxygen is a preponderating factor. The increased production of adrenal secretion in asphyxia is explained through the need of an increased supply of oxygen, and also of greater circulatory activity, to hasten the elimination of the carbon dioxide.

THYROID AND PARATHYROIDS.

As in the case of the adrenals, ample information is available concerning the phenomena which these organs may evoke, but the manner in which they incite them has remained obscure. Besides their familiar influence on growth and general metabolism, they are thought to oppose intoxication by toxic wastes and toxins; to cause general vaso-dilatation by increasing the excitability of the depressor nerve; to sustain calcium metabolism, and finally to promote katabolism of hydrocarbons. Analysis of these phenomena again shows that they can all be accounted for by a function which I attributed to these organs several years ago (1903–1907). Before reference to this function can be made, however, a few of the

data in support of the effects of the thyro-parathyroid secretion —granting that these organs act jointly, a fact sustained by considerable evidence—must be submitted.

As to metabolism, thyroid preparations have often been shown to raise the temperature, sometimes several degrees; to increase the oxygen intake and the carbon dioxide output sometimes over 20 per cent.; to augment nitrogen and phosphoric acid excretion, the latter sometimes very markedly. Graves's disease, we know, includes all these symptoms. Conversely, thyroidectomy lowers oxidation, the output of carbon dioxide, nitrogen, phosphoric acid, and other familiar symptoms of myxœdema. The effects of thyroid gland in the latter disease and cretinism sufficiently emphasize the influence of the thyroid on general metabolism.

As to the defensive rôle of the thyro-parathyroid apparatus, its importance is no less great. Its secretion had been shown by several observers to possess both antitoxic and bactericidal properties. The blood of thyroidectomized animals proved toxic—a condition relieved by the use of thyroid or thyroid grafts—while operated animals were extremely liable to infection. On analysis, I was led to conclude, in 1903,[55] that the thyroid took an active part *indirectly* in general immunity by increasing the functional activity of the adrenals, and, through these organs, general oxidation and metabolism; and, that the resulting increase of functional activity in those organs, which produced protective substances, correspondingly augmented in the blood the quantity of these substances—then known collectively as Buchner's alexins.

This view was confirmed experimentally at the Bacteriological Institute of Liége by Miss Louise Fassin.[56] In 1907, I then offered chemical evidence to the effect that the thyro-parathyroid secretion also acted *directly*, like Sir Almroth E. Wright's opsonins, *i.e.*, by sensitizing the pathogenic organisms, toxic wastes, etc., and thus preparing them for hydrolytic digestion. This also has been sustained. Léopold-Lévi and H. de Rothschild, of Paris, write in this connection in the second volume of their *Physiopathology of the Thyroid Gland*[57]: "Sajous has attributed, among the functions of the thyroid body, a *rôle* to the latter which he assimilates to that of opsonins and to autoantitoxines. More recently, Miss Fassin, M. Stepanoff, and M. Marbé have confirmed on their side the influence of the

thyroid on the blood's asset in alexins and opsonins."

How is this sensitization or "opsonization" produced? All clinicians know that the use of thyroid preparations in young cretins is sometimes attended by softening of the bones and bending of the legs, notwithstanding marked general improvement. When it is recalled that five-sixths of the inorganic matter of bone consists of calcium phosphate, it becomes a question whether the thyroid does not influence cellular phosphorus. That such is the case is further suggested by the facts that iodine, the active constituent of the thyroid secretion, and its salts, cause excessive elimination of phosphates and phosphoric acid,[58] and that thyroid preparations act in the same way.[59] "Emphasis must be laid," writes Chittenden,[60] "upon the apparent connection between the thyroid gland and phosphoric acid metabolism," giving as example "the increased excretion of P_2O_5 after feeding normal animals with thyroids, and the great decrease in the case of animals with the thyroids removed."

The untoward effects of large doses of thyroid preparations on the nervous system, owing to its wealth in phosphorus and fats, as manifested by tremor, tachycardia, optic neuritis,[61] etc., also bespeak such an action. Cyon,[62] in fact, found that injections of iodothyrin excite the depressor nerve directly to such a degree, that the vascular pressure often declined to two-thirds of the normal.

A familiar action of the thyroid preparations is a rapid reduction of fat in obese subjects, when full doses are administered. The presence in the fat cell of a nucleus rich in phosphorus, whose purpose is promptly to promote oxidation of the fat when the organism requires additional carbohydrates, explains this action. Schöndorff,[63] in fact, found that the reserve fats could be exhausted before the nitrogenous tissues were affected.

The mode of action of the thyroid active principle, iodine, is suggested by the presence of this halogen in all nuclei, as shown by Justus[64] and others. This means that iodine is found wherever phosphorus is present, while, as shown above, it is most active where phosphorus is known to be most plentiful. Now, chemistry furnishes a clue to the manner in which all the phenomena I have enumerated are produced. "If a fragment of phosphorus, lying on a plate, is sprinkled with iodine,"

writes Wilson,[65] "the substances unite, and heat enough is produced to kindle the phosphorus." Nitrogen, hydrogen, and chlorine are ubiquitous constituents of our tissues, and the vigorous explosives they form with phosphorus and the intense liberation of heat the reactions entail are familiar features of the laboratory. Roos found that, in a dog in nitrogenous equilibrium, iodothyrin "caused at once a marked increase in the output of sodium, sodium chloride, and phosphoric oxide."[66]

On the whole, these data appear to me to suggest that:—

The thyroparathyroid secretion enhances oxidation by increasing the inflammability of the phosphorus which all cells, particularly their nuclei, contain.

All pathogenic elements in which phosphorus is present, bacteria, their toxins or endotoxins, toxic wastes, etc., are thus rendered more vulnerable to the digestive action of the plasmatic, phagocytic or cellular defensive ferments.

The other effects of the thyroparathyroid product now find their explanation. By sensitizing the nuclei of all tissue cells, it enhances oxidation, and through it the vital process and growth. Its influence on calcium metabolism is accounted for by its action on phosphorus; it promotes the formation of calcium phosphate. It excites the depressor nerve by sensitizing its structural phosphorus. By this action, it also sensitizes the adipose tissue nuclei, and facilitates the katabolism of fats.

THE THEORY OF THE INTERNAL SECRETIONS.

As far as available evidence permits, the organs so far described seem alone to influence the entire organism through their products. No other organ has definitely been shown to produce an internal secretion capable of doing so physiologically, *i.e.*, under normal conditions. Pharmacological effects such as those obtained with pituitary gland or its extractives do not demonstrate the existence of a *bonâ fide* internal secretion. This applies also to the sexual glands, though here the presence of an internal secretion, limited normally in its action to the reproductive system including the mammary gland, is probable. Conversely, in the structures reviewed in this paper, we have what appears to me, when their functions are considered collectively and interwoven physiologically, *th fundamental mechanism of the vital*

and defensive processes of the body. Reduced to its simplest expression, this mechanism appears to me to be as follows :—

The thymus supplies to all tissues the excess of phosphorus in organic combination (possibly as nucleins) required during the development of the body, to build up its cell nucleins. The thyro-parathyroid secretion (thyroiodase) sensitizes these nucleins to the action of oxygen. The adrenal secretion (through its katalytic ferment adrenoxidase) endows the blood with its oxygenizing properties. The pancreas supplies the ferments which, in the intestinal canal and nutritional leucocytes, convert food materials into products harmonious to, and for the building up of, tissue cells, i.e., *for the anabolic phase of metabolism; the same pancreatic ferments carry on the katabolic phase of metabolism.*

All endogenous or exogenous substances which are not appropriate for tissue building—bacteria, toxins, toxic wastes, toxics, venoms, etc.—are subjected in the phagocytic leucocytes, the tissue cells, the lymphatic system and the blood plasma, to the katabolic phase of metabolism, which serves to convert them into eliminable end-products.

The defensive mechanism of the body thus forms part of its nutritional processes, the whole being dominated, as far as present knowledge enables us to judge, by the internal secretions reviewed.

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THYROID INSUFFICIENCY.*

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Definition.—The term thyroid insufficiency is applied to all morbid syndromes arising from abolition or diminution of the thyroid parenchyma; in other words, from inadequacy or suppression of the function of the thyroid gland. Where there is absolute lack of development or total extirpation of the gland, complete suppression of function ensues. This condition is described as "maximal" thyroid inadequacy. Where the thyroid secretion is reduced by infective, toxic or mechanical lesions, more or less complete derangement of one or more aspects of the thyroid function is the result. Under such circumstances, conditions of either "medium," or "minimal," inadequacy prevail.

Physiology.—The function of the thyroid gland is manifold. It controls the nervous system, the nutritional exchanges, and the humoral equilibrium. There is increasing evidence to show that it is in part responsible for the processes which I propose to describe as thermogenic, oregogenic,* morphogenic, antigenic and prophylactic.

There are disorders affecting some or all of these processes, which give rise to symptom-complexes of varying character. The origin of these syndromes, though more or less easy of recognition, has not until recently formed the subject of research.

General Definition of Thyroid Insufficiency.—Within the last few years, however, the notion of thyroid insufficiency has become very much broader in its application.

In the first instance, the term thyroid insufficiency was applied to extreme forms of the condition only. This was the

* "Nous désirons attirer l'attention sur une fonction du corps thyroïde que nous proposons d'appeler fonction orégogène, autrement dit fonction qui actionne les divers appétits," *Etudes sur la Physiopathologie du Corps thyroïde*, Octave Doin, 1908, p. 74. (Translator's note.)

logical outcome of the discovery by the Swiss school, that myxœdema resulted from spontaneous absence or surgical removal of the thyroid gland.

(2) At a later day, the term was extended to include partial or attenuated conditions, as well as the *formes frustes*. These belong to the category of slight thyroid insufficiency and are of far more frequent occurrence than the severer manifestations.

(3) More recently, however, the question has been found to be one of greater complexity than was at first supposed. Thyroid insufficiency, especially in its benign forms, is rarely pure. It is associated with a reaction to hyperactivity on the part of the gland, provoking a syndrome of by no means infrequent occurrence, which has been described by me in collaboration with H. de Rothschild under the name of thyroid instability.

(4) Having once established thyroid insufficiency and thyroid instability as clinical entities, it is possible to recognise in the subjects of these conditions the presence of other glandular syndromes, either existing in juxtaposition to thyroid insufficiency, or directly or inversely related to it. Whether it be cause or effect, in cases such as these thyroid insufficiency is frequently the dominating factor of the syndrome.

These four groups denote the system of classification which it is proposed to follow in the course of this article.

General Ætiology.— Before describing in detail the symptoms of thyroid insufficiency, it is expedient to give a brief summary of its ætiology.

Thyroid insufficiency may be the outcome of surgical intervention. Total extirpation of the gland is followed by myxœdema; that this is so is proved by the results of experiment.

In a case of cervical hypertrichosis, in which radiotherapy was employed, the thyroid gland became atrophied and the symptom complex of thyroid insufficiency was produced. (Acchioté). To these causes may be added the prolonged or unskilful employment of thyroid therapy in subjects of thyroid derangement.

Predisposition is at the bottom of all subthyroidic states.

It may be inherited (congenital debility as evidenced in subthyroidic families), or acquired, as the result of the intervention of other thyrogenic factors.

Attenuated or partial manifestations of thyroid insufficiency are the ones most frequently encountered, and these may affect persons of all ages, from sucklings to old people. They explain the entire symptom-complex of old age, and are observed with considerable frequency in infants, adolescents, and persons of mature age. The predominant rôle played by the thyroid gland in the sexual life of women, renders them peculiarly liable to the slighter forms of thyroid insufficiency.

In persons of low thyroid activity the precipitating causes of thyroid inadequacy are very numerous. Such are hygienic errors, a superabundance of meat in the dietary, over-feeding of any kind, venereal excess, and emotional excess.

There are a large number of maladies which exercise a debilitating effect upon the thyroid gland, and especially upon the impoverished thyroid gland. Of these, acute articular rheumatism, tuberculosis, and syphilis are the chief. It must not be forgotten, however, that under other conditions these diseases induce a predisposition to hyperthyroidism, which may even lead to Graves's disease itself. Other infective conditions which reduce the activity of the thyroid are: malaria, smallpox, scarlatina, dysentery, mumps, chicken-pox, whooping-cough, typhoid fever, influenza, erysipelas, leprosy, etc.

Intoxications of all kinds—alcoholism, lead-poisoning, mercurialism, verminous intoxication, etc.—are causes of thyroid insufficiency.

Thyroid insufficiency, as an expression of exhaustion, is a concomitant of Graves's disease, the condition thus presenting the successive stages characteristic of thyroid instability.

The incidents of the sexual life of women, puberty, menstruation, pregnancy, lactation, confinement, are also potent factors in the production of thyroid insufficiency. The influence of the menopause was described by Gull and Ord in the first works which appeared on myxœdema.

It is evident, then, that the causes which lead to diminution of the thyroid function are extremely numerous. Certain of these are underlying causes, and among them heredity is the chief.

Slight infections and transitory intoxications act as provoking causes upon an already impoverished thyroid gland. Indirect factors are sometimes manifested. Such, for instance, is renal inadequacy, which points to a pre-existing condition of latent thyroid insufficiency.

It frequently happens that the complete clinical picture of thyroid insufficiency is presented as the result of a combination of causes. The fundamental factor is supplied by heredity; the gland becomes further enfeebled by the action of toxi-infections; repeated pregnancies and lactation combine to reduce its activity still further; some minor factor, such as over-exertion or chill, is sufficient to provide the precipitating cause.

General Pathogeny.—It is not proposed to enter here into the results of suppression or absence of the thyroid gland. Medium or minimal thyroid insufficiency is a manifestation of reduced activity on the part of the thyroid parenchyma. The histology of the thyroid body is briefly as follows:—It is a sealed gland without excretory ducts, composed of vesicles separated by fine meshes of connective tissue, which enclose the arteries, veins, lymphatics, and nerves. Prolongations of the connective tissue are thrown out into the interior of the vesicles. The latter have a diameter which varies from 29 to 300 μ; they are entirely sealed, and are enclosed by a wall composed of a single layer of cells with clear nuclei. The cells are of two kinds, (cells with clear plasm and colloid cells), corresponding to the two different stages of secretion. The centre of the lobule is occupied by the colloid matter which results from the breaking down of the colloid cells.

In any condition of thyroid insufficiency, whether transitory or definitive, functional or organic, it is the noble element of the gland, the cell, which is affected. Speaking generally, there is derangement either of the quantity or the quality of the secreting substance.

(*a*) Atrophy of the thyroid gland, sclerosis of the connective tissue, from whatever cause arising, diminishes the quantity of the parenchyma.

(*b*) In so far as its secretory value is concerned, the cell may be in a state of congenital inferiority. It is known that the thyroid substance of debilitated

persons is poor in iodine contents. A simple congestion, whether of toxic, infective, or mechanical origin, may give rise to a cellular lesion or to weakening of cellular function, either condition being expressed by thyroid insufficiency. The glandular stimulation, by which numerous infections are accompanied, is frequently succeeded by a phase of secretory exhaustion. Does the nervous system play a part in the production of thyroid insufficiency? In view of Cottell's case, it is permissible to affirm that it does. Cottell observed myxœdema as the sequel to a bullet wound, which had destroyed the inferior cervical ganglion of the great sympathetic, together with the fibres extending to the thyroid.

Once insufficiency of the thyroid gland is established its secretory function, which is characterized chemically by the presence of iodine, phosphorus, sulphur, etc., becomes reduced; or, the resorption of the colloid substance and the products of internal secretion may be retarded.

The result in either case is general derangement of the organism. Disorders arise which are due to diminution of the soluble thyroid ferments in the blood, the oxidizing agents and the oxydases (catalase, peroxydase, lipase) (Yuchtenko).

CLINICAL STUDY.

The clinical conditions are: maximal thyroid insufficiency (myxœdema) and slight thyroid insufficiency.

A.—MAXIMAL THYROID INSUFFICIENCY (MYXŒDEMA).

Maximal thyroid insufficiency is expressed by the morbid condition to which Ord, in 1877, gave the name of myxœdema.

I do not propose to enter here into a lengthy account of this classic syndrome, which was first described by Gull (1873) and by Ord.

Apart from the infiltration, which is the characteristic symptom of the condition, myxœdema is expressed in childhood by a form of mental derangement which is commonly described as "idiocy of the cretinoid type"; by arrest of

development, which may amount to dwarfism; and by a general retardation of nervous activity and of the humoral exchanges. These symptoms are fully described in the text-books of the subject.

There are two points, however, upon which I should like to lay particular stress. The first is this: that in the causation of acute myxœdema, thyroid insufficiency, though the predominating factor, is not the only one. Among the endocrinic organs alone, rôles of varying importance are played by the hypophysis, the thymus, the testicles and the ovaries, as well as by the pancreas, liver, etc. Derangement of these organs reacts upon the tone of the nervous system and the great sympathetic, as well as upon the constitution of the blood-plasma. A portion of the symptomatology depends upon disturbance of these various glands. Briefly put, true myxœdema is a pluriglandular syndrome, the predominating feature of which is thyroid insufficiency.

The second point which I wish to emphasize has a particular application in adult myxœdema, the condition described by the earliest observers. In this form of myxœdema, the thyroid function is not suppressed; it is, however, sufficiently diminished to bring about infiltration and many other symptoms, such, for instance, as chilliness and falling of the hair. It may happen, however, that by a reactionary activity of the gland, local hyperplasia in the form of goitre is produced; and the signs of thyroid excess may thus exist side by side with those of thyroid insufficiency. Adult myxœdema is in reality a condition of thyroid instability having the appearance of myxœdema. I have seen ten such cases, and I find the experience they have brought me very valuable. Unless there is previous knowledge of the subject, the contradictory nature of the symptoms may lead to an error in diagnosis, with consequent error in treatment. Further, it is the co-existence in certain forms of myxœdema, of symptoms of hyperthyroidism which compels the employment of thyroid extract in minimal doses, and which renders a close scrutiny of its first effects so imperative. Where the drug is well tolerated, the signs both of thyroid insufficiency and thyroid excess, including goitre, disappear.

There are certain other points of interest in connection

with myxœdema.

In human pathology, ablation of the thyroid gland, especially that of children, produces the symptom-complex of myxœdema, including the characteristic infiltration ; and it is this fact which enabled the earlier Swiss surgeons to refer the condition, which until then was believed to be of nervous origin, to its true source. To obtain the syndrome experimentally by removal of the thyroid gland of animals, is a much more difficult matter. It has, however, been done by Horsley in monkeys, and by Gley in rabbits.

To recognize slight thyroid insufficiency in all its varied forms, an intimate knowledge of the maximal condition is essential. Any one of the classic symptoms of myxœdema may appear, frequently in a less intense form, in other morbid states. That such symptoms are of thyroid origin is proved by the favourable influence of thyroid medication.

Finally, even in cases where thyroid therapy is attended by the most satisfactory results, and effects a complete transformation of the subject, it is rarely capable of bringing about a radical cure. In the vast majority of instances the treatment must be continued indefinitely.

B.—SLIGHT THYROID INSUFFICIENCY.

In collaboration with H. de Rothschild, I have recently published a volume[1] on slight thyroid insufficiency. Owing to its frequency, and the favourable effect which suitable thyroid medication exercises upon the condition, the subject is one which deserves the attention of practitioners.

In view of the influence of the thyroid gland upon the nervous system, especially the vegetative system, and upon the humoral conditions, it is readily conceivable that insufficiency of the glandular function is attended by an extremely diverse symptomatology, the expression of which is determined, in the first instance, by local predisposition, whether inherited or acquired. The syndrome includes disturbances in varying degree of all the organs the function of which is subordinated to the sympathetic system ; which is, in its turn, dependent upon the activity of the thyroid gland.

The clinical aspects of slight thyroid insufficiency are,

[1] Léopold-Lévi and F. de Rothschild: *La Petite Insuffisance Thyroïdienne et son Traitement*, Paris, O. Doin and Fils, 1913.

however, more complex. To an even greater extent than is the case in uncomplicated myxœdema, slight or medium insufficiency is attended by a reactionary hyperfunction on the part of the gland, which is expressed by symptoms or syndromes of hyperthyroidism. In the second place, thyroid insufficiency is associated with symptoms arising from derangement of the other ductless glands.

To make the matter clearer, it will be best to classify the clinical signs, and to describe successively the following conditions:—

1. Uncomplicated slight thyroid insufficiency, without associated symptoms.
2. Slight thyroid insufficiency with concomitant hyperthyroidism.
3. Slight thyroid insufficiency associated with other endocrinic symptoms.

1. *Signs of Uncomplicated Slight Thyroid Insufficiency.*—Before entering upon a description of the symptoms of subthyroidism, there are one or two points to which it is as well to direct attention.

The signs of thyroid insufficiency are numerous, but they are rarely all present in the same individual. As a general rule, the symptoms are trifling, in the sense that they do not seriously affect the general health. Indeed, certain of them are so commonplace, that they fail to attract the attention of the physician. Taken singly, they are not characteristic of thyroid insufficiency, for they may arise from other causes, more especially from other glandular disturbances. Finally, symptoms of a general similarity may be produced by the opposite poles of thyroid activity. Thus, constipation may occur in both subthyroidic and hyperthyroidic states, as the result of thyroid atony or thyroid spasm. Vasomotor derangement consistently combated (vaso-dilation, passive or active) may bring about headache of either subthyroidic or hyperthyroidic origin.

The facts which have led me to regard as significant the slighter symptoms of thyroid insufficiency are as follows:—

(1) That these symptoms are present in myxœdema;

(2) That they yield to thyroid medication;

(3) That the reverse symptoms are observed in Graves's

disease ;

(4) That these reverse symptoms may be produced by means of thyroid extract given by the mouth.

The presence in an individual of the slighter signs of thyroid inadequacy constitutes what may be called the sub-thyroidic temperament. These signs are as follows :—

1. *Transitory Infiltration.*—Apart from the presence of cardiac or renal affection, a white indolent œdema, which does not pit on pressure, makes its appearance in the vicinity of the eyelids, the forehead, and the cheeks ; occasionally, there is transitory swelling of the feet, and the subject finds that his boots are temporarily too tight for him. Or the fingers may become sufficiently swollen to render the removal of the rings a matter of difficulty. This transient œdema occurs with varying frequency ; it may or may not be periodic in its occurrence, and it is observed in the earlier part of the day, or as the result of worry, fatigue, menstruation, migraine, or an asthmatic attack.

2. *Hirsute Derangements.* — Such are partial congenital alopecia, capillary nanism, premature baldness, premature greyness. The eyebrow sign is most important ; it consists in absence or premature falling of the eyebrows, or rarefaction or disappearance of the outer third. It is referable either to what Hertoghe describes as a process of "*keratose pilaire*" or to defective development (*agénésie pilaire*).

3. *Caloric Disturbance.*—(*a*) In its most attenuated form, this manifests itself as coldness of the extremities, especially of the feet. It is frequently unconscious, particularly in children, or it may be subconscious.

(*b*) A second form appears as chilliness, either general, or confined to one or other of the extremities, or localised in the back or thighs. The sensation is conscious, the patient making frequent complaints and employing measures of all kinds to guard against it.

(*c*) A third manifestation is shivering fits, which come on after meals or in the earlier part of the day. They may be momentary, or they may be prolonged and accompanied by chattering of the teeth and trembling of the whole body.

(*d*) The temperature as measured by the thermometer is frequently several points below the normal, especially at

night.

(*e*) People with subnormal temperatures are frequently exquisitely hypersensitive to cold (Hertoghe). The slightest draught provokes rheumatoid or neuralgic pain, or brings on a lumbago, torticollis, or migraine.

4. Chilliness is associated with *vasomotor derangement*, of which aero-asphyxia, cyanosis, and chilblains are the manifestations. The pulse is usually small and slow.

5. An intestinal symptom which is the stamp of the subthyroidic temperament is *constipation*. Like the preceding symptoms, constipation is a feature of myxœdema and is susceptible to thyroid treatment.

6. *Fatigue*, especially matutinal fatigue, is very common. Subthyroidic people are usually loth to get up, and they are not at their best in the morning. They usually brighten after they have breakfasted and have begun to move about. These subjects sometimes say that they were "born tired."

7. *Anorexia*.—Subthyroidic children have rarely much appetite, and this is frequently the case with adults. They have to be forced to eat and eating gives them no pleasure. This symptom improves, sometimes to a surprising extent, under the influence of thyroid extract.

8. *Somnolence*.—Subthyroid subjects require a great deal of sleep, and they fall asleep readily after meals. Thyroid extract frequently has a marked effect in reducing the need for sleep.

9. The subthyroidic temperament is associated with a tendency to *obesity*; in other words, the subject possesses a nutritive orientation which, under the influence of exogenous conditions, such as an over-abundant dietary coupled with insufficient exercise, predisposes to the formation of fatty deposits.

10. The *skin* is dry, rough, harsh, thick, scaly, and ichthyotic.

11. The *stature* is small, generally below the medium. The subject has either always been small, or has ceased to grow as the result of some illness which affected his thyroid gland.

12. Certain developmental processes are *retarded* (dentition, walking, speech); sometimes development of the testes, brain, hair, teeth, etc., is arrested.

13. On the other hand, there is sometimes a tendency to

premature senility. It is manifested by varicose veins, hæmorrhoids, excessive development of the veins of the hand, a tendency on the part of the teeth to loosen and come out, premature baldness and greyness.

14. Subthyroidic persons are subject to *muscular* and *articular pain*, and to frontal and occipital headache. The latter is more severe in the morning, and is so persistent that they end by becoming accustomed to it.

15. To these must be added apathy, indolence, and depression, the combination uniting to form the syndrome of *partial neurasthenia* (*neurasthénie fragmentaire*).

16. The *eyes* are frequently deep-set, small, atonic, and lacking in expression ; they resemble glass-eyes.

17. Viewed as a whole, the subthyroidic temperament is characterized by *attenuation of the vital reactions* and *diminution of the nutritional exchanges.*

The nutritional derangement is expressed in the conditions affecting the urine. There is diminution of diuresis, as well as in the amount of the contained substances. There is increase of uric acid, excess of ammonia, and increase of Lanzenberg's coefficient of acidosis.

It is exceptional to find all these signs present in one individual. The greater the number, however, the greater the likelihood of their disappearance under thyroid medication. Let us imagine for an instant a case in which all the signs are present. The subject will be small in stature, with a tendency to obesity ; his extremities will be cold and cyanosed ; there will be partial congenital baldness ; the hair will be fine and prematurely blanched ; the eyebrows will be very scanty. There will be infiltration of the face, especially in the neighbourhood of the eyelids, and the skin will be harsh and dry. The observer will be struck by the dull expression of the eyes and by the slack, depressed, and apathetic bearing. Closer examination will reveal the fact that the appetite is poor, the bowels constipated, the pulse slow ; that the nails and teeth are in a wretched condition ; that there is a tendency to headache, somnolence, muscular pain, and chilliness. In such a subject the thyroid body is not visible during either effort, repose, or deglutition, and it cannot be located by palpation.

The signs of thyroid insufficiency which have been

described, and which may be regarded as the stigmata of the condition, develop only in organs and in systems which already possesses a certain predisposition. Even more than the multiplicity of the thyroid function, this fact is responsible for the variability of the clinical picture as displayed in different individuals. It sometimes happens that accentuation of a local predisposition leads to the development of an extra-thyroidic syndrome, a morbid complex which, in some cases, may fitly be termed a malady, of which thyroid insufficiency is the underlying cause. For example : thyroid insufficiency is accompanied by muscular fatigue, partial neurasthenia, an ichthyotic condition of the skin, and alopecia. Now, the degree of neurasthenia, myasthenia, ichthyosis, diffuse alopecia, may far exceed that which characterises the symptoms of thyroid insufficiency, yet these signs may be due to thyroid insufficiency, and in that case will respond to thyroid treatment.

Thyroid inadequacy is further accompanied by other indirect results. The activity of the thyroid gland in the production of opsonins and alexines is reduced, with the result that the organism becomes very susceptible to slight cutaneous and mucous infections, as well as to auto-infections, such as recurrent sore throat, recurrent herpes, skin troubles, etc. Subthyroidism provides a favourable soil for recurrent erysipelas, a condition which yields readily to thyroid medication.

In the same way, the antitoxic activity of the thyroid gland is reduced, and the auto-intoxication which results is no doubt the underlying factor in such processes as urticaria, œdema, migraine, etc. Eczema, psoriasis and other skin affections are referable to the same cause.

2.— SLIGHT THYROID INSUFFICIENCY WITH CONCOMITANT HYPERTHYROIDISM.

Simple inadequacy of the thyroid is rarely observed clinically, but is almost invariably associated with symptoms of thyroid excess.

The association in one individual of the signs of subthyroidism with those of hyperthyroidism constitutes the condition, which, in collaboration with H. de Rothschild, I have called thyroid instability. The clinical aspects and manifestations of the condition are manifold.

In some instances, a person of hyperthyroidic temperament

becomes, from a variety of causes, subthyroidic in habit. The former condition is expressed by the large stature, the good condition of the hair and eyebrows, and the history of nervous irritability. In such an instance, the instability is arrived at by successive stages.

In other cases, though the underlying condition is subthyroidic, it is associated with hyperthyroidic reactions. Here the hyperthyroidism is derivative or reactionary. It is possible, even, for both phases to exist simultaneously in the same apparatus (*e.g.*, temperature, hair) as the result of hyperthyroidic exacerbations, which, without modifying the habitual morbid signs (coldness of the feet, baldness) yet induce the appearance of symptoms diametrically the reverse (waves of heat to the face, hypertrychosis of the eyebrows). In such a case, the instability is best described by the term "homopragic."

It may happen, again, that among the many functions of the thyroid gland, some are deranged in the direction of subthyroidism (chilliness, constipation, lack of development of the eyebrows), while others have undergone modification in the reverse sense (palpitation, trembling, exophthalmos, nervousness). The condition is one of "homochronous" thyroid instability. The symptom-complex may supply evidence of the inclusion, among the apparatuses affected, of the great sympathetic or the pneumogastric; of vagotonic or sympathetico-tonic participation in the condition of thyroid inadequacy.

The hyperthyroidism associated with thyroid inadequacy may be classified in the following manner:—

(*a*) Paroxysmal derangements of a hyperthyroidic nature, which appear as simple reactions and may be classed as symptoms.

(*b*) Reactions of a more complex character, the manifestation of which includes other symptoms, and which may be classed as syndromes.

(*c*) Reactions affecting the thyroid gland itself (endogenous goitre).

A. *Slight Symptoms of Hyperthyroidism.*—These constitute the prevailing characteristics of Graves's disease, and may be

provoked by means of thyroid given by the mouth.

In character, they are the reverse of the slighter symptoms of thyroid insufficiency, and may be briefly described as follows :—

1. Hypertrichosis, more particularly of the eyebrow.
2. Hyperthermia, flushings, febricula of thyroid origin.
3. Acro-erythrosis, with cutaneous humidity.
4. Tendency to diarrhœa, the stools being soft and frequent.
5. Great physical restlessness, with a sensation of being hurried.
6. Insomnia.
7. Emaciation.
8. Excessive height.
9. Developmental precocity.
10. The syndrome which I have named "syndrome of persistent juvenility."
11. Extreme nervous irritability, with cardiac and cutaneous excitability, etc.
12. Large, brilliant, protruding eyes, with nystagmiform movements.
13. The reactions are generally excessive, and there is exaggeration of the nutritional exchanges.
14. Hyperplasia of the entire thyroid gland.

These symptoms are rarely united in the same subject, and this is especially true of the class of case under consideration, namely, subjects in whom the fundamental condition is one of thyroid instability, the glandular inadequacy being partial. The ideal hyperthyroidic subject presents the following classic features. He is tall, with a tendency to leanness; there is vasomotor disturbance, manifested in acro-erythrosis with dampness of the skin; the eyebrows are bushy and meet in the centre; the entire capillary system is very much developed; the eyes are brilliant and widely opened, with nystagmiform movements. All the functions are intensified, hence there is rapid pulse, exaggerated appetite, repeated evacuation, and frequent micturition. The hyperthyroidic subject is nervous, suffers from palpitation, irritability, excitability, trembling of the body, insomnia. These phenomena sometimes make their appearance during emotional crises and,

in women, at the menstrual period.

B. *Hyperthyroidic Syndromes* (*Thyroidolepsy*).—Associated with thyroid insufficiency is a large number of syndromes, the characteristic features of which are, that they are precipitated suddenly in the form of thyroid crises, and that they yield to treatment with thyroid extract.

Although associated with thyroid inadequacy, these syndromes are the clinical expression of a hyperthyroidism which is, in itself, the reactionary manifestation of the fundamental subthyroidic condition.

They are: migraine, ophthalmic migraine, asthma, nasal asthma, attacks of chronic rheumatism and gout, mucous enteritis, urticaria and other skin affections (acne, eczema), mental symptoms.

These diverse symptoms are united in a condition which, in France at any rate, is accepted as classical, namely, neuro-arthritism. For my own part, I believe that neuro-arthritism is of endocrinic origin, and that, in many instances, it is the expression of thyroid inadequacy associated with paroxysms of hyperthyroidism.

C. *Endogenous Goitre.*—The association in the same subject of the signs of hyper- and hypothyroidism is expressed by changes in the thyroid gland itself. These modifications, which are chiefly observed in women, assume different forms.

The extreme manifestation is slight goitre.

The medium form is expressed subjectively by neuro-arthritic conditions, though here, also, there is always goitre.

In the benign form, inspection and palpation of the neck during the process of deglutition will reveal inequality with partial hypertrophy of the thyroid body.

OTHER ENDOCRINIC SYMPTOMS ASSOCIATED WITH THYROID INSUFFICIENCY.

Other symptoms are frequently associated with those of thyroid insufficiency, and certain among these depend for their manifestation upon the derangement of other ductless glands.

The important points are these:—

1. The symptoms in question are not necessarily asso-

ciated with thyroid insufficiency.

2. They may form part of the clinical complex, not of subthyroidism, but of hyperthyroidism.

3. They are associated with lesions or derangements of other endocrinic glands, and these lesions or derangements are capable, on their side, of primary or secondary reaction upon the thyroid body, giving rise either to thyroid insufficiency or to secondary thyroid instability.

Among the most important of these derangement, are those affecting the male and female genital functions.

In men, thyroid insufficiency is accompanied by (*a*) imperfect development of the sexual organs, including uni- or bilateral cryptorchidism; (*b*) diminution of sexual appetite.

In women, the genital disorders arising from thyroid insufficiency are very numerous, and may be summarised as follows: Late puberty, as the result of a kind of ovarian instability dependent upon the thyroid; premature puberty; amenorrhœa; momentary tardiness, insufficiency, or suspension of menstruation; precocious suppression of menstruation; genital dystrophia, such as uterine infantilism, either partial or complete; displacements, including anteflexion and lateroflexion, anteversion and retroversion (the result of imperfect development of the posterior uterine wall), together with infantilism of the ovary and permanent atrophy of the Graeffian vesicles. Signs of premature uterine regression and hyperinvolution of the uterus are sometimes observed; these correspond to a kind of infantile regression or premature senility of the uterine apparatus.

The subthyroidic state is sometimes associated with disorders of a purely functional character, which yield to treatment with thyroid extract. Such are irregular menstruation, menorrhagia, metrorrhagia, genital instability, menstrual pain, and certain types of leucorrhœa. Sterility and repeated abortion are also included in the signs of thyroid inadequacy.

It is hardly necessary to repeat that, among the arguments in favour of the association of these genital signs with thyroid insufficiency, the strongest is the fact that they yield to thyroid medication.

Thyroid insufficiency, whether partial or complete, is some-

times associated with excessive development of the mammary gland, in men as well as in women. This may be accompanied by hypertrophy of the parotids. Hypertrophy of the parotids, with concomitant hypertrophy of the lachrymal glands, constitutes Mikulicz's syndrome, which has been observed in connection with thyroid insufficiency.

The function of the liver is, to a certain extent, subordinate to the thyroid function, and hepatic derangement is a frequent outcome of thyroid insufficiency. In connection with the biliary conditions, the following points are of interest: the possible passage into the urine of the colouring substance of the bile; the toxicity of the biliary salts of the urine; icteric pruritus; chloasma; and, probably, catarrhal jaundice. The coincidence of biliary lithiasis with thyroid insufficiency has been remarked upon by several observers. The glycogenic (hepato-pancreatic) function of the liver is affected by the hyperfunction of the pancreas, by which thyroid insufficiency is usually accompanied. It thus acquires an increased capacity for the fixation of sugars, except in excessive quantities. By improving the hepatic conditions, thyroid medication reduces the alimentary glycosuria in myxœdema of certain types.

Ammonia, which is normally converted into urea in the liver, is present in excess in the urine of the subjects of thyroid insufficiency.

Hæmorrhages, arising from reduced coagulability of the blood and poverty of fibrogen, are among the disorders of thyrohepatic origin.

To hepatic derangement is undoubtedly due the diminution of the antixenic function, that is to say, of defensive activity against infective disease. In a very interesting work, Müller points to the intimate association of the liver and the thyroid in the formation of alexines and natural antibodies. The function of the secretion of these products devolves upon the liver, while the thyroid pours into the circulation the substances which are calculated to excite this secretion.

The hypophysis is occasionally concerned in the production of a symptom-complex, which is associated with thyroid insufficiency, is sometimes accompanied by testicular insufficiency, and is manifested by a disproportionate development of

the extremities.

The participation of the suprarenal in a symptom-complex of endocrinic origin is revealed by reduction of arterial tension, with abnormal pigmentation and muscular asthenia.

The association of these various derangements with thyroid insufficiency produces syndromes which are described as pluriglandular. They are very numerous, but I have limited my description to those which are dependent upon a condition of thyroid insufficiency. As a matter of fact, it is essential in any case of thyroid insufficiency to distinguish between those symptoms which are directly of thyroid origin, and those which depend upon the derangement, in various ways and as the result of thyroid inactivity, of other organs and functions.

In certain physico-pathological complexes, such as senility, a large part is played by thyroid inadequacy. Senectitude is essentially an attribute of subthyroidism, though other glands (testes, pancreas, etc.) are equally involved in its production. It affects every tissue of the body, but its influence upon the entire endocrinic system is very far-reaching and profound.

Forms of Thyroid Insufficiency.—Thyroid insufficiency is expressed in a certain number of conditions, which are distinguished from one another by the combination of their symptoms, by their intensity, by certain etiological factors (age, sex, endemicity), and by the association of certain other factors.

These conditions may be briefly described as follows :—

Incomplete myxœdema, which may also be described as Hertoghe's syndrome.

Endemic cretinism, which depends upon the association of thyroid inadequacy with genital disturbance.

Infantilism, with secondary testicular or ovarian insufficiency.

Senilism, which is a complex syndrome, partly of subthyroidic origin.

Developmental retardation, cerebral, dental, piliary, osseous (nanism).

Paroxysmal subthyroidism, brought about by sudden chill, menstruation, excessive emotion, etc.

Minimal subthyroidism, which corresponds to the subthyroidic temperament.

Thyroid insufficiency, of every degree, is sometimes expressed by partial, diassociated syndromes, which result from the derangement of certain aspects of the thyroid function to the exclusion of others.

Finally, the association of symptoms of thyroid insufficiency with disorders connected with the hypo- or hyperfunction of other endocrinic glands, produces pluriglandular syndromes, the complex dysendocrisias to which reference was made in the early part of this article.

Evolution of Thyroid Insufficiency.—Thyroid insufficiency is, as a rule, insidious in its onset. When the condition has set in during infancy, its nature is frequently perceived in retrospect at a later stage. Occasionally it appears as the sequel to an acute malady, or as the outcome of Graves' disease. Once the condition is established, it may remain stationary; it may undergo spontaneous amelioration; it may develop in the direction of myxœdema, or in that of hyperthyroidism (thyroid instability); or it may be susceptible to treatment by thyroid extract.

As a general rule, the evolution of thyroid insufficiency is a matter of time, though manifestations of the condition may be of a transitory, paroxysmal, or periodic character.

Among the conditions in which thyroid insufficiency may terminate, the most important, with the exception of myxœdema and Graves's disease, are arteriosclerosis and premature senility. To these must be added contraction of the palmar aponeurosis, which is a kind of local senility and responds favourably to thyroid medication.

Prognosis.—Apart from the sequelæ mentioned above (arteriosclerosis, premature senility), thyroid insufficiency does not, as a rule, threaten life. It is frequently the expression of a condition which has been mistaken for arthritism, and is grave only in so far as the multiple effects of auto-intoxication are concerned. It must be pointed out, however, that thyroid insufficiency does not offer a favourable soil for the development of tuberculosis.

Speaking generally, subthyroidic persons are the victims of many and various evils. They are often ailing, rarely ill; and they tend to make the most of their ailments.

The condition is very amenable to treatment. Concomi-

tant hyperthyroidism (pregnancy, emotion, febrile diseases) may, by spontaneous reaction of the gland, act as an actual auto-therapy.

Diagnosis of Thyroid Insufficiency.—Diagnosis is of extreme importance, for on it depends the employment of efficient treatment.

Thyroid insufficiency should always be suspected in the case of a person presenting neuritic and arthritic syndromes, or showing any of the symptoms of hypo- or hyperthyroidism; in gouty people; in the subjects of retarded development; in women who suffer from menstrual troubles, etc.

Signs of thyroid insufficiency should be sought for in all toxic infections, in all endocrinic complexes, and wherever it is desired to determine the temperament of the subject.

Where thyroid insufficiency is suspected, it is very necessary that a careful search should be made for all the clinical signs of the condition. The discovery of a single symptom is not sufficient, in itself, to establish a diagnosis.

Having established the diagnosis, it should be confirmed by treatment with thyroid extract. This is essential, for even in the case of manifestly subthyroidic subjects, the usual accompaniments, such as adenoid growths and incontinence of urine, are not necessarily of subthyroidic origin, and they may even prove refractory to thyroid treatment. When the results are immediate, continued, constant, and pronounced, they may be regarded as a diagnostic factor.

In the case of pluriglandular syndromes, the results of thyroid treatment serve to distinguish between symptoms of thyroid origin and those provoked by derangement of other endocrinic glands. Even in cases where thyroid insufficiency is proved, the endocrinic balance must be maintained and the coexistence of other endocrinic insufficiences and instabilities (testicular, ovarian, parathyroid, suprarenal, pituitary) must be allowed for.

Treatment.—The method of treating thyroid insufficiency is, essentially, by means of thyroid substance given by the mouth. Preparations of the whole gland should be employed. I prefer a preparation of the healthy gland, cold-dried in a vacuum. The question of dosage is a very difficult one. It may be accepted as a general rule that, while subthyroidism

is the foundation for a thyroid treatment, the dosage is regulated by the concomitant hyperthyroidism. Of the dry preparation, which is equal to about five times its weight of fresh gland, I employ doses which vary from 1 millegr. (about $\frac{1}{64}$ gr.) to 3 centigr. (slightly less than $\frac{1}{2}$ gr.). For the sake of convenience, the powder is put up in cachets containing 1 mg. ($\frac{1}{64}$ gr.), 5 mg. ($\frac{5}{64}$ gr.), 25 mg. ($\frac{25}{64}$ gr.) and ·1 g. (about $1\frac{1}{2}$ grs.). After examination of a patient, the first thing is to arrive, as nearly as possible, at the optimal dose, which is limited by the formula : never too little, never too much. Whatever the initial dose, it should at first be given three times a week, then four times, then five times, up to ten times. The quantity of the dose is next increased, the same gradual procedure being followed. After each ten days, it is advisable in most cases to suspend the treatment for from three to five days. It should always be suspended during menstruation.

The pulse and the weight should be watched, and a careful look-out should be kept for the appearance of nervous symptoms. The effect of the treatment in modifying certain symptoms is, in some instances, positively magical. It is pertinent to ask, at what age should thyroid therapy be instituted ? The earlier, the better. Remarkable results are sometimes obtained with infants. The treatment may be employed with advantage in the case of old people, though with this reservation, that the drug must be exhibited in small doses. The duration of treatment varies with the nature of the syndrome. In chronic rheumatism, it may be continued for months or even years. Speaking generally, it should be continued for as long as it remains effective. Having been suspended, it may be again resumed should the untoward symptoms reappear.

In slight thyroid insufficiency, thyroid medication appears to act directly upon the thyroid gland itself. Thyroid extract either stimulates or regularises the thyroid gland, according to the amount of the dose. It may be that it acts directly upon the nervous system, sympathetic or autonomous, or it may influence the hormones independently of the nervous system. The hormones have a direct stimulatory action, independently of the mediation of the nervous system, upon

other endocrinic glands and upon various organic tissues.

It is very expedient that other clinical measures, appropriate to the condition of the patient, should be employed in conjunction with thyroid therapy. Attention should be given to general hygiene, the hygiene of the skin and of the intestines, respiratory hygiene, and the discipline of the nervous system. Little meat food should be taken, and cold baths should be avoided. Among drugs, bicarbonate of soda promotes the activity of the thyroid gland. Strychnine will be found useful in the case of debilitated subjects, valerian for the nervous.

Treatment with thyroid extract may be modified or reinforced by the employment of certain other methods (metathyroid). Such are, iodine, arsenic, sulphur, phosphorus, calcium, and soda. To these must be added sea-air and certain forms of treatment called thermal.

Where thyroid insufficiency is associated with other endocrinic insufficiencies, the glandular therapy should be equally complex ; ovarian, testicular, suprarenal, and pituitary extracts may all be employed with advantage in suitable cases.

THE PANCREAS.

By PROFESSOR CARL von NOORDEN, M.D.

THE theory of the internal secretion of the pancreas has an important historical bearing upon the development of modern biological doctrines. The suggestion, as a matter of fact, had often been made that the blood obtains special chemical substances, not only from ductless glands, such as the thyroid, but from the glands with ducts as well. Only the liver, however, was definitely known to be a gland endowed with bi-polarity of its cells, producing bile on the one hand, and sugar, among other bodies, on the other. The ingenious Brown-Séquard, in 1869, had maintained this polarity in cell-function, and had tried to explain in this way some of the phenomena of uræmia, but he did not furnish any conclusive proof of it. Even his impressive researches into the effects of testicular extract only helped a little at first towards the general adoption of the idea of the internal secretions; their great and principal importance has only been appreciated at a much later day.

I. DIABETES FOLLOWING COMPLETE REMOVAL OF THE PANCREAS.

The scientific ground was thoroughly well prepared in 1889, when J. von Mering and O. Minkowski for the first time produced, by removal of the pancreas, an experimental diabetes, which in all essential points resembled the spontaneous affection in man. We must not forget to recognize the work of the Italian investigator, de Dominicis, who independently carried out similar experiments at the same time, and arrived in principle at the same results as the authors mentioned; although the matter was not worked out so fully and fundamentally by him as by von Mering and Minkowski. Consequently, his investigations remained of little influence upon the development of the point in question.

To begin with, the most important facts are:—

1. When the pancreas of a dog is completely removed,

severe diabetes is produced on the following day at latest, and definitely reaches its maximum 48 hours afterwards; the animal dies in the course of a few weeks. The attack must be deemed "severe," because glycosuria persists although the animal receives no carbohydrates; even fasting does not cause it entirely to disappear. The disease in the maimed animal resembles the severe disease in man in such details as chronic glycosuria, polyphagia, polydipsia, polyuria, hyperglycæmia, wasting, loss of strength, excretion of large quantities of acetone, aceto-acetic acid, β-oxybutyric acid, and ammonia, as well as death from coma. In addition to the discoverers, several investigators have engaged in the further study of pancreatic diabetes; some of these have not been able to confirm the original statements in full, because they were not always successful in producing glycosuria, or else it was only present for a short time after the operation and never developed into actual diabetes. Minkowski, however, proved conclusively that all failures in results can be explained by faulty methods of experiment. There are, indeed, great difficulties in the technique of the complete removal of a dog's pancreas. If the removal is not complete, the incidence of diabetes cannot be expected.

Experimental diabetes after complete removal or destruction of the pancreas has been found possible, up to the present, in the following animals:—Dogs, cats, pigs, monkeys, frogs, tortoises, and carnivorous birds. In the case of fish, the information varied, and that obtained from graminivorous birds—ducks and geese—was similarly indefinite. There is much more hyperglycæmia, but no glycosuria. Why these birds do not excrete the excessive sugar from the blood, is still not clear; probably, it is closely connected with the mechanism of the secretion of urine. Up to the present, most of the data have been obtained from dogs, and it is to these that the following remarks refer.

2. When more than one-tenth of the gland is left behind in the body in functionable condition, diabetes does not ensue; on the other hand, the digestion and absorption of food, especially of fat and proteid, may be impaired very considerably, because too little pancreatic juice reaches the intestine. If nearly one-tenth is left, there is at first slight

diabetes. The glycosuria is trifling, and only appears after ingestion of carbohydrates. But, as the result of the injury to the parenchyma and the vessels, the small remnant of the gland very often becomes diseased and degenerates. Then, commensurate with the progress of the degenerative process, the initial slight diabetes is developed to a more intense degree, and, finally, is just as severe as it would be after immediate total removal—the so-called Sandmeyer's diabetes.

3. The importance of the pancreas to the sugar-content at any rate in dogs, appears to be "specific," that is, the total removal of no other organ produces the same results, and after the pancreas has been removed, no other organ can vicariously replace its missing functions. Some writers, certainly, have stated that complete removal of the salivary glands gives rise to glycosuria. Suitable and careful control-experiments by Minkowski show that this does not occur with cautious and painstaking operations. The same thing was maintained still more insistently with regard to resection of the duodenum and dividing the mesentery, so that the idea of pancreatic diabetes seemed to be compromised seriously, when duodenal diabetes was recognized by so great an authority as E. Pflüger. Eventually, however, it was found that resecting the duodenum only causes diabetes, if, owing to the difficulties of the operation, the closely adjacent pancreas is, at the same time, badly injured and becomes necrotic. On the other hand, the fact must be recognized that operations in various parts of the body, and particularly when they are associated with great pain to the animals, can set up a temporary glycosuria. This, however, passes off again in a few hours, or at most after a few days. It is probably connected with direct or reflex irritation of the sympathetic system, and is akin to Claude Bernard's puncture-diabetes. Nevertheless, nobody has ever seen genuine progressive diabetes appear after removal of any organ other than the pancreas.

4. The external secretion of the pancreas has nothing to do with the characteristic disturbances of the sugar-content. The whole of the pancreatic juice may be excluded from the bowel, for example, by ligature of the excretory duct and

other methods. This occasions serious loss in absorption, and the general nutrition of the animal suffers considerably, but no trace of diabetes is found. The auto-transplanting of the pancreas affords the strongest evidence. The gland is loosened from its bed, and one portion is resected, whilst the other, supported by its afferent and efferent blood-vessels, is fixed to the abdominal walls in such a way that the external secretion runs away outside, and can no longer reach the gut. At first, no diabetes occurs, but if afterwards the sutured piece of pancreas is removed, now a slight operation, then the animal at once becomes diabetic.

In many of these experiments, all the nerve-supply of the pancreas has been destroyed in the transplanting, but this in no way makes any essential difference to the result. To this fact are referred those, who would trace the developing diabetes back, not to the loss of the gland-substance, but to the injuries to the nerves inevitable in the operation. In order to make the proof still more precise, part of the pancreas was first removed, and then planted in the spleen of the animal, quite free from its original nerves and vessels. Naturally, no diabetes was produced. As soon as it could be assumed that the transplanted portion had coalesced in some measure with its new environment, the rest of the gland was removed. Even then, there was no diabetes; that only appeared when the transplanted portion was removed, or when it gradually became necrosed, or was absorbed, which always takes place in the long run.

By dint of all these and similar experiments, which now for more than a century have claimed the attention of eminent observers, the original conclusions of von Mering and Minkowski have been proved to be right.

> Either, some substance is accumulated in the organism, after removal of the pancreas, which is detrimental to carbohydrate metabolism; or, after this operation, some substance or function is lacking which normally serves to promote carbohydrate metabolism.

These formulæ serve as comprehensive but vague methods of expression. As a matter of course, the second formula is

looked upon as more likely to be right, and, in course of time, this opinion has hardened into a dogma. To be just, we must admit that in accurate knowledge of biochemical detail, we have not, at the present day, got much beyond what these cautious and carefully drawn up propositions assert. The discovery was not only of importance to the theory of diabetes, but, further than that, it acquired a fundamental significance for the whole theory of internal secretion, which would have remained in its infancy without the knowledge of pancreatic diabetes.

II. HOW DOES THE PANCREATIC HORMONE ACT?

If, owing to removal of the pancreas, an internal secretion, a hormone, is wanting, which is of definite importance in carbohydrate metabolism, then we are at once confronted with a crowd of new questions. These, to-day, can only be answered by hypotheses, for even the normal conditions of sugar-metabolism are still in no way clear.

The pancreatic hormone has not as yet been isolated. It was, naturally, first sought for in the pancreas itself, but all the research has been nugatory. The hope of obtaining a substance out of the gland, which, just like thyroidin, could replace the diseased and inadequate organ, has not been realized. Obviously, the hormone is only produced in mass, as it is wanted and utilized; there is no storing up a reserve, as in the production of urine by the kidneys. Some experiments seem to show that the hormone, partly at least, reaches the lymph-stream in the blood-vessels. If the thoracic duct is divided, and its stream diverted out of the body, then dogs get slight glycosuria.

This proves, therefore, that sufficient hormone does not now arrive where it is wanted. Moreover, the curative effect of chyle can be proved in experimental and in human diabetes: in the former, the result is slight and by no means free from criticism; in the latter, there is hardly any effect at all. A more likely place, perhaps, to look for the active substance would be the blood of the portal vein, in view of the fact that it is chiefly made use of in the liver. Into the lymph-channels of the liver, and beyond into the thoracic duct, will probably be excreted only the residue for which the

liver has no use.

Where is the field of action of the hormone? Where does it carry out its decisive influence upon the process of sugar-metabolism?

An analogous theory assigns the seat of glycolysis and the point of attack of the hormone to the pancreas itself. But, it seems, pancreatic tissue has by no means any stronger glycolytic action than most other organs. Glycolysis, as proved by digesting glucose in the pulp of organs of many different kinds, can now be traced to the presence of oxidizing ferments, distributed over the body. No separate function, such as the possession of a glycolytic or diastatic ferment, attaches to the pancreas.

A theory, never accepted, which was propounded simultaneously and independently by O. Cohnheim and R. Hirsch, has been revived. It is to the effect that, as a matter of fact, neither the expressed juice from the pancreas alone, nor that from muscles alone, has any glycolytic action, but that a combination of both juices is actively glycolytic. From this the biochemical importance of the pancreatic hormone appeared to be known, and considerable progress seemed possible. But G. Emden was unable to confirm the principal facts by control-experiments carried out with the greatest care in my Frankfort laboratory, and could indicate the source of errors. He was supported later on by many other physiological chemists, but C. W. Hall obtained results agreeing with Cohnheim's. Although Hall's very exact work is not open to doubt as being analytically correct, yet his results do not prove that specially active glycolytic processes cause the disappearance of sugar. The work of Levene, Starling, and others shows that, in digesting sugar with the expressed juice of organs, condensation products (double-sugar) are formed, which simulate the disappearace of sugar. Levene treated the digested mass with dilute hydrochloric acid; this split up the newly-formed bi-saccharide, and he recovered the original amount of sugar.

Knowlton and Starling approached the same question in another way. They passed blood, previously made diabetic by removal of the pancreas, through the heart of healthy dogs and the like. In normal hearts, very large amounts of sugar disappeared from this during its passage, but in a diabetic

heart, only very little. The addition of pancreatic extract to this blood caused the disappearance of sugar, even in diabetic hearts. The beautiful experiments of this distinguished investigator appear, therefore, to prove that, in the first place, the presence of pancreatic extract is necessary for the decomposition (oxidation) of the sugar in the blood ; nevertheless, the huge consumption of sugar by the healthy heart is indeed puzzling.

Levene's work gave Starling the opportunity to revise his conclusions, although he had enunciated these much more lucidly than the other. In his communication to the International Medical Congress in London, Starling considered that his original interpretation of his results was not correct, and proved that the greater part of the sugar in a healthy heart may be conveyed by polymerization of a higher order in carbohydrates. The conclusion that the working muscle does not attack and decompose any sugar without the influx of pancreatic hormone, cannot therefore be drawn from Starling's and similar work.

In a paper just published, M. Landsberg arrives at still more definite results than Starling. He closes his article (*Deutscher Archiv f. klin. Med.*, Vol. 115, p. 489), with these words :—"From all that has been said here, it is clear that there can be no question about a direct proof of the reduction, let alone the removal, of sugar-combustion in a diabetic organism. My results are the following : the blood-cells of depancreatized animals decompose just as much sugar as those of normal animals ; normal blood-cells in the serum of depancreatized animals use up just as much sugar as the blood-cells of normal animals. Normal blood-cells in the serum of depancreatized animals consume no less sugar than in the serum of normal animals. The sugar-consumption of the working muscles of animals with pancreatic diabetes corresponds throughout in its gross amount to that of normal animals. The facts here published tell unquestionably against the need of the pancreatic hormone for sugar-consumption by means of parenchymatous cells. It is probable that this hormone is only of definite importance for carbohydrate metabolism in the liver."

For a long time, Lépine's theory held the field. He

believed that he had discovered that, after removal of the pancreas, the blood loses in glycolytic ability. Consequently, sugar accumulates in the blood, and from this hyperglycæmia glycosuria is derived. Lépine's results were chiefly of importance in so far as they removed the decomposition of sugar from the blood, thus contradicting the views hitherto current. Several observers, well skilled in biochemical methods, tested Lépine's experiments afterwards, but could not confirm them, so that, for some time, in fact Lépine's theory has been relegated *ad acta*. It turns up again with certain modifications in Meyer's works, but the part of his industrious research dealing with this question does not appear to me to be very conclusive. On the other hand, he establishes firmly that pancreatic extract has the property of making the renal filter impervious to sugar as a physiological condition, but it is very unlikely that he is dealing with the same hormone that is wanting in diabetes, for in human diabetes impermeability of the kidneys for sugar increases sooner. For instance, there are many cases, in which by suitable dieting, glycosuria can be stopped completely, but when the blood is examined in this aglycosuric stage, we are surprised at the large amount of sugar present. From 0·20 to 0·23 per cent. of sugar is often found, an amount, therefore, at which sugar would certainly be excreted by a healthy person.

Minkowski himself has hardly developed this original thesis further. In all his writings, he only emphasizes more incisively than at first, that the real trouble, after removal of the pancreas, is due to the fact that, in becoming diabetic the organism has lost the capacity for decomposing and utilizing sugar. Many authors, myself among them earlier, have arrived at the same conclusion, because of the degree of the respiratory quotient in severe diabetes of men and animals.

When carbo-hydrates are oxidized in the body into end-products, CO_2 and water, in non-diabetics the respiratory quotient amounts to 1.

$$\frac{CO_2 \text{ produced}}{O \text{ consumed}}$$

The more albumen, and, above all, fat, is oxidized, the nearer it approaches to 0·7. As a matter of fact, only the

fat is concerned in this, for the proteid metabolism, at least under normal conditions, is much too small to influence the height of the respiratory quotient to any appreciable extent. In normal men, when fasting, the quotient is on average 0·85, a sign that the body still possesses a reserve stock of glycogen. The longer fasting is kept up the nearer the amount of 0·7 is approached, because when the reserve glycogen is used up, the organism only has fat and albumen to deal with as sources of energy. On the other hand, after taking in carbohydrates, the quotient jumps upwards and approximates to 1, because carbohydrates are preferred by the tissues as soon as, and as long as, they are present for use.

We now find in severe diabetes the following variations of these normal conditions.

1. The quotient, when fasting in the morning, always remains below 0·8, values of 0·75 and less often being found.

2. After ingesting starch or glucose, the quotient does not rise at all, or only very slightly, and it makes no difference whether the body is at rest or being actively exercised.

Hence, it has been concluded that the carbohydrates could not be oxidized, but this assumption was hasty, and is most likely wrong; in any case, it is not convincing. The constant level of the quotient only affords the same information, that fat serves as the material for the production of the variations in energy; but we understand nothing at all about the intermediate metabolic processes. If fat is the source of the sugar in the blood, then the respiratory quotient ought to be of the type of fat combustion as well, if the muscles do not seize directly upon the fat, but only on the sugar originating from fat (in the liver). The question whether sugar can originate from fatty acids is a recognized theme for lively discussion. With regard to this, I have shown, for over twenty years, in fact, that the laws of energy demand an affirmative answer to to this question, but the chemical proof is wanting. J. Embden was the first in recent years to indicate in his writings the chemical method.

I cannot go more deeply here into this interesting and important question of the formation of sugar from fatty acids.

It only remains to me regarding it to emphasize that the characteristic condition of the respiratory quotient in diabetes permits of many explanations, and thus, in strict logic, cannot be looked upon as proof of the incombustibility of sugar.

It is quite clear that all the theories advanced up to the present, proceed on the assumption that in diabetes the consumption of sugar in the tissues may be reduced. The want of the pancreatic hormone should have made it impossible, or at least extremely difficult, for the tissues to attack and decompose the glucose molecule—that is, their normal food. This inadequacy of glycolysis naturally presupposes that other distributors of energy are attracted to the working of the liver, and in particular to the functional power of the muscles. Opposed directly to this self-evident postulate, which is much too often forgotten, is the fact that all direct experiments to prove reduced glycolysis, either in the blood or in the tissues, have been failures (*cf. supra*). Moreover, physiology has only just made known to us that the active muscle consumes carbohydrate ; on the other hand, the knowledge of the splitting up of other substances, especially of fat, by muscle is a blank page. Everything that has been adduced to the proof of deficient glycolysis is either refuted by careful control-experiments, or admits of another interpretation.

I have put the question to myself in this way : Are not the disorders of metabolism in diabetes capable of explanation, if the glycolysis remains intact?—that is to say, if the capacity of the tissues, especially of the muscles, to consume sugar is not injured in any way. This brought me dead against all modern theories of diabetes, and led back to the old, long-forgotten hypothesis of Claude Bernard and Chaveau-Kaufmann, that diabetic hyperglycæmia is caused by original overproduction of sugar in the liver. This theory was certainly not tenable or admissible in the form advanced at that time. If we adopt this point of view, the question of disordered glycolysis is eliminated for us. *We do not consider the glycolytic process as being morbidly reduced, but the diastatic process as being abnormally increased.* The term "diastatic process" refers, however, in accordance with the customary use of language, simply to the splitting up of highly organized carbohydrates, starch and glycogen, and covers a small part only of the whole process of

sugar-formation. We can, therefore, put it more aptly by saying that we look upon the total sugar-production as being increased, with the result that the blood is flooded with more sugar than can be consumed, and that part of this excess flows away through the kidneys. Out of what material the glucose in the blood is formed, we leave absolutely doubtful. The chief seat of sugar-formation is most certainly the liver, which, under normal conditions, suits the supply simply to the demands of the tissues. This demand controls the production of sugar. These are physiological facts which are beyond dispute. Our theory of diabetes goes thus far: in diabetes, the control is abrogated; consequently, the production of sugar is unrestrained.

Latterly, we have learnt to recognize the adrenals, as well as the pancreas, as an organ which wields an influence on the production of sugar. How can we explain the influence of the two organs? Each has an opposing action. In the pancreas, it is the deficiency; in the adrenals, it is the excess of the specific hormone that leads to the production of sugar. This suggests the idea, that the sugar-factory (*Zuckerwerkstatt*) in the liver is under double control. It is depressed by the pancreatic hormone, chemically unknown at present, and is stimulated by adrenalin. The joint effect of the two antagonists insures the normal output of production.

Until now, experimental experience has taught that adrenalin certainly induces vigorous, but only transient, stimulation in the sugar-factory. Many kinds of ephemeral glycosuria can be explained thereby, particularly the strange cases of transitory neurogenous glycosuria. The artificial glycosuria caused by Claude Bernard's puncture belongs to this class as well; the irritation proceeds from the medulla through the sympathetic to the adrenals, and causes an overflow of adrenalin. But, at present, there is no fact which entitles us to trace a chronic glycosuria—that is, true diabetes—back to chronic hyperadrenalism. The only disease, in which we often find actual chronic hyperadrenalism in the blood, is contracted kidney, and that again clearly stands in definite clinical contrast to diabetes; for very often glycosuria is reduced, or even disappears altogether, when contracted kidney comes on. What is said here, concerns the severe, as well as the mild,

cases of diabetes. I consider it a grave error to make any qualitative distinction between the mild and the severe cases of diabetes. Both are of the same nature; the differences are only quantitative and the transitions are fluent. Unfortunately, this is not taken sufficiently into account, with the result that mild cases are not treated with enough consistency. It is true, indeed, that a mild case of diabetes can remain continually mild, and never acquire a tendency to exacerbation; but, for the most part, slight glycosuria is the early stage of the severe form of the disease, and, in order to limit further development, everything must be running smoothly.

We do not, therefore, accept hyperadrenalism as the cause of true diabetes. Apancreatism is so much more important than hypopancreatism. The weaker the specific function of the pancreas, so much the less is the process of sugar-formation kept under control. That being abolished, the production is no longer adjusted to the needs of the tissues, but goes on without restraint, measure, or limit. Excellent material is squandered. In mild cases, only the actual diastatic process is concerned—that is to say, the wasteful action only attacks carbohydrate (glycogen); in severe cases, all material, the chemical nature of which can serve as a source of danger, is dragged into the whirlpool (sugar-formation from albumen and fat, glycosuria in fuller abstraction of carbohydrates). There is, therefore, abnormal irritability and abnormal stimulation in the sugar-factory, notably the liver. All degrees occur, from the slightest hypopancreatism in which only a very marked defect (food rich in starch, etc.) leads to overstimulation and overproduction up to most complete apancreatism—very severe diabetes.

We assume that the harmful effect of removal of the pancreas does not inhibit the further decomposition of the glucose molecule, but promotes the disintegration of the early grades of glucose—amylolysis, proteolysis, lipolysis. The word amylolysis is here used for decomposition of glycogen; one could as well say glycogenolysis. We are thus brought back, as previously stated, to the simple theory of overproduction. The seat of overproduction can only be the liver, which is known, as a physiological fact, to be the only organ in which new formation of sugar actively takes place. Only in the

liver does the outgoing blood contain more sugar than the incoming. That sugar formation of local importance can take place in other places as well, cannot therefore be denied; it occurs unquestionably in the muscles and leucocytes—disposal of the glycogen deposited in the cells, and general diffusion of the diastatic ferment. The cause of the over-production of sugar in the diabetic liver is the loss of the pancreatic control. If we denote the whole mechanism of sugar-formation localized in the liver as "sugar-factory," we can, for greater lucidity, state it in these terms: the irritability of the sugar-factory is increased by loss of the pancreatic hormone. There are present irritants which impel the factory to mobilize much more sugar than was demanded by the stimuli. Of these, physiology recognizes three.

1. *The stimuli, which come from the alimentary tract,* require the digestion of the absorbed material—carbohydrate and proteid. How much they control glycosuria in diabetes is acknowledged.

2. *As to the stimuli which issue from tissues in need of sugar.* Every exchange of energy in the body is associated with sugar-consumption. The greater this exchange the more sugar must be mobilized and conveyed to the tissues. It may be said quite generally that every increase of total metabolism increases the sugar-production of the liver as well. The indications which reach the liver are probably of a chemical nature. In severe diabetes, we have the surprising phenomenon that glycosuria is increased by loading the total metabolism, such as by hard muscular exertion, pyrexia, and the effect of external cold. According to our theory, this implies that the stimulus reaching the liver occasions in that over-sensitive sugar-factory, much too strong a stimulation and effect. On the non-oxidation theory, the increase of glycosuria, so abundant in fatiguing muscular exertion, was quite inexplicable. That is the so-called "cold diabetes."

3. *The mobilization of adrenalin* in the liver, when a physiological influx, does not cause any diabetes, but sudden increases of the inflow give rise to excessive hyperglycæmia and glycosuria (*cf. supra*, neurogenous glycosuria). Single injections of 1 mg. of adrenalin in healthy dogs, and in many normal men, cause slight glycosuria for one or two hours.

The effect is always reduced by repeating the injections. After removal of the pancreas, the effect of adrenalin is increased. The influence of the pancreas in counteracting the adrenalin has ceased. If we often see in diabetes that strong nervous stimuli actually cause a temporary increase of glycosuria, then we ought to trace this back as well to positive adrenalin action. After loss of the pancreatic hormone, the liver is defenceless against hyper-adrenalism.

The specific metabolic disturbances in diabetes are explained by the theory of over-production just as well as by that of non-oxidation ; still better and with less straining are some of the facts in the pathology of the disease, such as the retention of sugar in the blood, the neurogenous increase of diabetic glycosuria, the influence of sleeplessness upon glycosuria, and the increase of glycosuria due to fatiguing muscular exercise. The explanation of acetonuria is the same in each theory.

One is constantly asked, too, about the evidence for the over-production theory. At present, positive proofs cannot be adduced. They are, indeed, hardly to be expected, until chemistry has yielded us full understanding of the connection between decomposition of fatty acids and the origin of sugar. Both problems are knitted up indissolubly one with the other. To prove this here, would take us too far. On the other hand, we are aware of two facts, which directly contradict the non-oxidation theory, but accord well with ours.

1. If, in a non-diabetic animal, the liver is removed, or is ligatured in such a way that no more venous blood passes from the liver into the circulation, the respiratory quotient immediately rises to 1. That is, only the carbohydrates now available are consumed; other oxidizable materials, like fat and proteid, are no longer obtainable for the supply of sugar to the blood, and can have no effect upon the respiratory quotient.

2. In dogs, diabetic after removal of the pancreas, the respiratory quotient is at first 0·7 (*vide supra*). If this were the result of non-oxidation of sugar, then the quotient should remain just as low as after ligaturing the liver. This is not the case, it rises much more promptly than in non-diabetic animals. Yet, only carbohydrate is consumed. The source

from which the sugar in the blood arises, and which causes the low state of the quotient (fat) is now exhausted.

These researches, which were carried out by my former assistants, H. Salomon and O. Porges, decidedly contradict the non-oxidation theory, and support the theory of over-production. They were made with so much care, that there can be no doubt about their correctness. Others who tested the experiments—Versár, Grafe and Rolly—did not exclude the liver as completely from the circulation as Salomon and Porges. They found, in consequence, an actual increase of the quotient after the operation, although it did not rise to 1. Or they tried to give another interpretation to the results (Rolly), but in view of the perfectly clear results, that is difficult to establish. As a matter of course, these experiments must still be continued. I believe it will be easy to obtain a result altogether free from objection and perfectly definite, if the determination of the respiration is not made in a whole animal, but by making use of the so-called "muscle-animal"—that is, with complete removal of stomach, intestines, and liver, and decapitation—and comparison of the respiratory quotient in animals with and without a pancreas (Carrel's method).

(2) The most recent experiments of Starling and Patterson (*vide supra*) showed, in full agreement with the findings of Salomon and Porges, that, in spite of removal of the pancreas, sugar is destroyed in the muscles. This was proved still more conclusively by the experiments of M. Landsberg.

It may still further be stated that the function of the pancreatic hormone is specific; that is, that it cannot be replaced by any other organ or secretion. This is not negatived by the fact that intimate relations exist between the pancreas and other glands with internal secretion, notably the thyroid and the pituitary body. From both glands emanate stimuli of a chemical nature, which, to a certain extent, limit the action of the pancreas. Just as the pancreas checks sugar-production in the liver, so these two glands tone down the pancreas. The stimulus is certainly not strong enough to nullify the action of an histologically intact pancreas, but for all that, it is enough to make itself clinically obvious under certain conditions. The glycosuria

that apparently often results from the medicinal use of thyroidin, may be brought to mind, as well as many cases in which Graves's disease and acromegaly—hyperthyroidism and hyperpituitarism—are associated with diabetes. These are examples of multiple disease of the vascular glands. In these combinations, the glycosuria invariably has something characteristic: it tends to be very fluctuating, and does not depend upon a change of diet by any means so directly as in uncomplicated disease of the pancreatic island-system.

On the contrary, it is known that deficient function of the thyroid and pituitary body counteracts the onset of glycosuria. Enormous quantities of glucose can be given in typical myxœdema and in pituitary obesity, without giving rise to glycosuria. This is explained by the assumption that in hypothyroidism and in hypopituitarism there is a cessation of the inhibitions that act upon the pancreas, with the result that the elimination of the pancreas hormone is increased. These effects can be obtained as well with the sugar in the blood. Even when glycosuria does not occur in hyperthyroidism and hyperpituitarism, an increased amount of sugar is almost invariably found in the blood-picture; on the other hand, in myxœdema and in adiposo-genital degeneration, the amount is for the most part below normal.

Everything here adduced about the nature of the action of the pancreatic hormone cannot be claimed to be demonstrable by biological investigation. The theory of the internal secretions is still of recent origin. Every year brings fresh surprises, but, on the basis of newly found facts, it is already necessary now to revise and reject without hesitation from the old theories and hypotheses all that does not agree with the new facts. It was for this reason that I devoted myself in some degree more closely to the old theory of "disordered glycolysis," and on further examination everybody will agree with me in the conclusion that only age and custom uphold it, and that the foundations on which it was first erected have one by one crumbled away. Whether the theory of overproduction, which I now advocate, will remain as I first presented it, the future must show. In any case, a topical interest attaches to it.

For further information about the questions here discussed,

I refer to my monograph, "Modern Aspects of Diabetes," published by Treat and Co., 1912, and my communication to the International Medical Congress, London, 1913, section VI., p. 237.

III. LOCALIZATION OF THE DIABETIC LESION IN THE PANCREAS.

It has already been mentioned, that the metabolic disorder in diabetes is completely independent of any affection of the external pancreatic secretion. In fact, one often sees cases of very severe diabetes in which the specific digestive functions of the pancreatic juice are perfectly maintained. On the other hand, there are cases in which the discharge of pancreatic juice into the gut is wholly abolished, and nutrition is impaired by steatorrhœa and creatorrhœa, without presenting the least symptom of any diseased carbohydrate metabolism. This proves, indeed, that the secretory cells of the pancreas are not the seat of the diabetic affection. Certain experimental experiences prove this assumption.

The opinion was first expressed by Laguesse, in 1893, that the so-called Langerhans's islands may be the seat of the internal secretion of the pancreas. These islands are structures with a thoroughly characteristic morphology, which sharply differentiates them from the acini. It was of the greatest importance when Opie found an actual atrophy of these elements in men who had died of diabetes. Several hundreds of careful microscopical examinations by many prominent anatomists have confirmed this; above all, Weichselbaum in Vienna and Herberg in Copenhagen have done excellent work in this direction. One can to-day agree with the opinion of both these observers: no diabetes without disease of Langerhans's islands.

With regard to the relations of the islands to the acini, no complete unanimity obtains. Two opinions exist:—

1. The islands are certainly connected anatomically with the rest of the pancreatic tissue, and are supplied by the same blood-vessels; but they have nothing to do with the acinous tissue. One structure never passes over into the other. Their functions are different from beginning to end. In the testis and ovary, there is a similar local union of two entirely different tissues. In these, the generative portion of the glands is

embedded in the so-called Leydig's interstitial tissue, but they have a totally different development and function.

2. A second view is held, that the islands are an early stage of the acini. The old acini gradually die, and are replaced from the islands. So long as the early form is present it provides the internal secretion ; later, after the change into acini, the tissue then produces the external secretion, whilst new islands appear in its place. This idea is more and more losing ground.

Here it is necessary to enter no further into this conflict of ideas. Each year brings new evidence that it can only be in the islands that the internal secretion of the pancreas arises. Heiberg has stated positively that quantitative relations exist between the severity of the diabetes and the number of islands. Apparently, that is going too far, for other investigations show that the functional incompetence of the island system can depend upon qualitative change as well, and, on the contrary, is not always proportional to the number.

IV. RELATIONS OF HUMAN DIABETES TO THE PANCREAS.

I have advocated the point of view that in every case of real diabetes, there is a functional breakdown of the pancreas. Since then, after v. Mering and Minkowski had demonstrated this supposition by the discovery of experimental pancreatic diabetes, nearly all modern investigators of diabetes have come to the same conclusion, some earlier, some later. Pathological anatomy, just as emphatically, has helped essentially the revolution of opinion. At first, it was not possible in any way to prove *post-mortem* in the majority of diabetes cases structural changes in the pancreas. The pancreas in typical cases of diabetes often proves to be normal in size, consistency, and colour. Even microscopical examination showed no actual variations. I can call to mind numerous autopsies, at which my honoured master and friend, Carl Weigert, declared after careful investigation : "I find no pathological changes in the pancreas."

Comparatively often in diabetics, one finds sclerosis of the smaller arteries of the pancreas and chronic interstitial pancreatitis. The appearance of diabetes in alcoholism and in old-standing syphilis is thus explained. Calculi were often

found in the pancreatic duct, associated with severe inflammatory conditions and necrosis of the tissues surrounding the duct. Diabetes was found much more rarely in the case of cysts in the pancreas, and particularly so in cases of cancer of the pancreas. D. von Hansemann explains this on the hypothesis, that the new proliferating cells of the neoplasm preserve the biological properties of the mother-cell, and continue to supply the internal secretion (altruism of the cells).

At any rate, the positive anatomical *post-mortem* findings could not fully satisfy the supporters of the pancreatic theory, nor refute the opponents, until attention was called to Langerhans's islands. Then it was first shown that a pancreas may appear quite normal on macroscopic inspection, and that it may be possessed of a definite apparatus for external secretion, whilst at the same time grave changes are found in the interspersed system of islands. Most commonly there are found a reduced number of islands (Heiberg), decrease and shrinking of the islands, hyaline swelling of the parenchyma with indistinct nuclei (Weichselbaum). The latter calculates that in non-diabetics about 4·3 per cent., and in diabetics on an average only 1·2 per cent. of the total pancreas-mass escape from Langerhans's islands.

In severe diabetes ("pure" diabetes, deaths from diabetes), one should be certain of finding in almost 90 per cent. of the cases thoroughly characteristic histological changes in the islands; in slight diabetes (death from complications in the earlier stages of the disease), the most experienced observers, like Heiberg and Weichselbaum found changes in from 40 to 50 per cent. of the cases. If, therefore, it must be admitted that gaps in the proof are still present, then the evidence now submitted is at least quite conclusive enough. We must remember that the use of more delicate histological methods is only of recent date, further refinements of these, such as new stains, will probably realize still greater gains.

In any case, we have to content ourselves with the probability that there are functional lesions of the islands as well, which never reveal themselves to the microscopist. This reminds us, therefore, that we must admit as well functional lesions of the pancreas, which do not at all depend upon disease of the gland itself, but are caused by inhibitions

proceeding from other glands with internal secretion (thyroid, pituitary). But in actual diabetes, these certainly do not play any great part; at most, it would seem, that the remarkable fluctuations of glycosuria, which are met with in complications with Graves's disease and in acromegaly, are conditional on the variations in intensity of that influence (*see above*).

It appears to me to answer the present position of the investigation, if we say; the intensity of diabetes is inversely proportional to the total quantity of Laugerhans's islands present in good functionating condition. Heiberg had, as mentioned before, laid the chief importance upon the "number" of the islands, but this can hardly be maintained.

If we recognize inadequacy of the islands as the cause of deficient internal secretion of the pancreas, and, in the long run, of diabetes, then we must acknowledge that two totally different groups of diseases can be the basis of diabetes.

1. *Diseases of the islands, which are brought about by diseases of their environment.*—In these, we include cases, in which the islands are sympathetically affected by acute or chronic pan-pancreatitis. These inflammatory conditions are either of metastatic origin (purulent pancreatitis) or proceed from Wirsung's duct. In this group, too, must be included the serious disorders of nutrition of the whole parenchyma of the gland, which depend upon pancreatic arteritis (*see* above), as well as the rare cases of diabetes in encapsuled abscess in the pancreas, in pancreatic cysts, and in primary or metastatic cancer of the pancreas. In all these cases, it is not a question of a systemic disease of the islands, but of casual injuries, against which the islands, even if originally quite sound and vigorous, are defenceless.

2. *Systemic disease of the islands, that is, specific disease of the islands independently of the surrounding tissues.*—About the nature of these diseases, which obviously predominate in frequency and are almost exclusively in question in the typical severe forms, especially diabetes of infancy and of youth, nothing is yet clear. Still, however, there is already something of greater probability to record.

a. Congenital constitutional atony of the island system.—This is co-ordinate with the congenital atony of other systems with internal secretion, for instance, congenital atony of the

interstitial part of the generative glands, eunuchoidism, hypogenitalism, infantilism; congenital atony of the thyroid, myxœdema in children, cretinism, predisposition to endogenous obesity and tendency to subsequent myxœdema. When the family history of a diabetic is carefully traced out, it will often be found that diseases of the internally secreting glands have frequently appeared. It is not diabetes always, but account has to be taken as well of diseases of the thyroid—Graves's disease, juvenile obesity, myxœdema, cretinism, struma; of diseases of the pituitary body—acromegaly, dystrophia adiposo-gentalis; of diseases of the adrenals—Addison's disease; of diseases of the accessory thyroids—tetany; of diseases of the spleen—pernicious anæmia, hæmatogenous jaundice; of diseases of the generative glands—eunuchoidism (in men), hypogenitalism (in women), sterility, etc.; and of diseases of the thymus. The records I have already obtained show, in this respect, that we shall have to hand, in the same statistical collection, trustworthy material showing that atony of the vascular gland system is hereditable to a remarkably high degree. It is now this and now that system that is concerned in individual cases; sometimes it is one, sometimes many systems (polyglandular inadequacy). It is, however, atony of the pancreatic island-system that is mostly in evidence.

In many cases, the pancreatic island-system is so predisposed to atony, that under no conditions does it respond to the demands. It has already been exhausted prematurely by the normal physiological burden of work, and disorganized by degeneration and atrophy (diabetes of children and young people). In other cases, a certain capacity for resistance exists, which protects the individual from the disease. Not until after more than ten years of apparently normal function does asthenia arise. Whether in these cases, the disease breaks out, or not, apparently depends mostly on this, to what extent the organ is called upon and burdened. According to our theory, the greater the load and therewith the likelihood of wear and tear, the more considerable is the consumption of carbohydrates and proteids. For to the stimuli which these foods carry to the sugar-factory of the liver, the internal secretion of the pancreas has directly to act as a

check. If, therefore, in hereditary tendency to diabetes we advise moderation in the supply of carbohydrates and *fats*, and the incorporation, as much as possible, of the requisite energy in the shape of proteids, we shall thus, in the most rational way, transfer a verified axiom of the treatment of diabetes to the prophylaxis of the disease.

b. Acquired atony of the island-system. — In other cases, the congenital weakness of the island-system is not enough to allow diabetes to develop under the sole influence of load and wear and tear. Special dyscrasiæ must affect the system. Of what kind, then, are such lesions? The ground for a discussion always becomes more ill-defined, but it appears to me, that one important fact before all others must be noticed and taken into consideration: the dependence of lesions in the parenchyma of the islands upon infectious diseases. Cases, in which diabetes has developed in the train of measles, scarlet fever, streptococcal angina, influenza, and malaria, more and more accumulate. Apparently, it is a specific parenchymatous lesion of the islands, analogous to, for instance, nephritis after scarlet fever or angina, orchitis following mumps, myocarditis subsequent to many infectious diseases.

These meta-infectious lesions of the islands certainly do not seem to be beyond recovery. I have already reported a case, some time ago, of a child who became diabetic soon after scarlet fever, but got quite well again in the course of a few months. In another case, very severe diabetes with a great deal of acetonuria, came on after measles. In common with all the other physicians, I had quite given up all hope, but I heard, a short time ago, that complete recovery had occurred quite spontaneously. In view of these experiences, I have begun to have the tonsils removed in diabetics, whose history specifies frequent attacks of tonsillitis. Up to the present, three cases have been treated in this way, but no opinion on the therapeutic result can be offered until some time later.

Even from other toxins, partly of the exogenous and partly of the endogenous kinds, such as intestinal toxins, serious lesions of the pancreatic islands must be apprehended.

Whether a thoroughly healthy island-system can be

affected under the influence of the infections above-mentioned and of others not yet noted, or whether a certain (congenital) constitutional weakness of the island apparatus must already be present beforehand (Pfaundler's *disease-readiness*), cannot yet be answered. But now, there already exists some hope that we are leaving that most unsatisfactory stage, in which it is said: diabetes is a constitutional disease of unknown origin, in which we reply to every patient, who asks about the cause of his illness, with a *non liquet*. We can now no longer connote diabetes as a general metabolic anomaly, but have to recognize it as a totally distinct organic disease, which certainly results in serious metabolic disturbances by reason of the supreme importance of the functions involved.

V. THERAPEUTIC CONCLUSIONS.

The modern interpretation, herein set forth, of the diabetic process throws light as well upon recognized therapeutic practices. We learn to appreciate that many cases of diabetes have no decided tendency to improve, because the process in some of the islands has ended in destruction. The unimpaired residue by no means suffices to control completely the sensitiveness of the sugar-factory; it can only avert hyperglycæmia and glycosuria in greater or less degree. When a certain load is exceeded, there is some limit of tolerance to the glycosuria. Patients, in spite of this glycosuria, feel very well, and this lasts for some time, several years, ten or more. The uniform healthiness is mostly a temptation to gross negligence in diet. Although in isolated instances even this does no harm, yet in the majority of cases the continuance of the well-being cannot be sustained.

In some patients, the gradual accession of the damage caused by this neglect is limited to complications. We have every reason to suppose, that these are closely connected with the confirmed hyperglycæmia. Then, the recognized and dreaded diabetic complications set in very often in individuals who have persistent hyperglycæmia by reason of ingesting carbohydrates in too large quantities, although not the slightest symptoms of diabetic auto-intoxication (acidosis) can as yet be detected: neuritis, neuralgias, cataract, pruritis, furunculosis, and so forth; I include as well with these the

premature appearance of arterio-sclerosis. The very same abnormal conditions of nutrition, which persistent hyperglycæmia engenders, promote the early wear and tear of the vessels. This accounts for the great frequency of general arterio-sclerosis, of sclerosis of the cardiac vessels, of vascular contracted kidneys, and of peripheral gangrene in diabetics.

It may be asked: how then are such disorders of nutrition possible, when the tissues obtain at the least rather too much than too little of their main food (glucose), and when must we give up the old idea that they cannot use this sugar? Can, then, the important new work upon one-sided nutrition and "partial under-nutrition diseases" (deficiency disease, C. Funk), give us perhaps a hint? For the cells, glucose is the most usual and by far the most suitable food. If that is persistenly present in excess (diabetic hyperglycæmia), then a kind of compulsion is exercised in the tissues to force them to make use of more sugar than they are accustomed to. The deluge of sugar prevents the cells from absorbing, fixing, and digesting other important substances in sufficient quantities. One may say: the excess of sugar drives away from the food of the cells materials which have for the cells the importance of the so-called "vitamines," and, consequently, there is brought about earlier exhaustion of, and less power of resistance in, the tissues. Both these features are characteristic of all diabetic complications.

In other patients, the complications do not persist, but a decline of tolerance finally sets in; that is to say, that the still existing residue of pancreatic islands gradually loses its former functional capacity (may be owing to anatomical lesions or perhaps to functional). Everyone who has large experience of the treatment of diabetes, will agree that this deterioration of tolerance is increased and accelerated by unsuitable loading with carbohydrates, and that it can be warded off, or at least appreciably kept down, by means of judicious limitation of carbohydrate.

Even in cases in which the original destructive process in the pancreas has stopped and in which, therefore, the diabetes has in the first place no progressive feature, the island-system is altogether of less value. If we introduce much carbohydrate, much pancreatic hormone is wanted as well. By

extravagant ingestion of carbohydrate, we spur the weakened secretory organ in an unprecedented fashion, like a tired horse out of which we wish to extort the last reserves of strength. Is this possible in other glands? The modern treatment of nephritis comes to my mind, in which, in my opinion, the holding back of the so-called "kidney-irritants" is carried much too far, often so far that the whole nutrition of the body suffers severely in consequence.

If the physician is mindful of the fact, that every loading up with carbohydrates burdens the hormone secreting glands of the pancreas as well, he will approach with more intelligence the old, and yet again the very modern, problem of the treatment of diabetes. He will give the diabetic as little carbohydrate as possible, that is, no more than he actually requires for keeping in good condition, and after careful determination of the tolerance in each case, he will order the amount to be allowed by measure. If the degree of tolerance is not known, it is impossible to be certain whether the amount prescribed for the individual case is correct or not.

The direction, that the loading of the island-system must be reduced to a minimum, is obviously still more requisite in those cases in which the whole island-system is originally of little value (hereditary constitutional anomalies). Then, too, a tendency to exacerbation is almost always present. This mostly occurs in those cases which we are obliged to trace back to infectious-toxic influences (specific systemic disease of the islands, *see above*). All hope, therefore, is centred upon the favourable influence which, empirically, the utmost care of the organ will exert. The sooner we begin, indeed, the better.

It is therefore of the greatest importance to bring the early stage of diabetes under the strictest diabetic treatment at once, and not to comfort oneself and the patient with the idea that only a "passing alimentary glycosuria" or a "trivial neurogenous glycosuria" is present. The latter certainly can be insignificant (transient adrenalinogenous stimulation); but an alimentary glycosuria, which makes its appearance under conditions in which the average healthy man excretes no sugar, is never unimportant, but always indeed the symptom of pancreatic inadequacy, that is, a diabetic predisposition.

In these stages, it is still possible to protect the weak organ

by far-reaching and persistent management, and to prevent the outbreak of a well-marked diabetes. As yet, unhappily, this happens all too seldom. The old method of treating diabetes is still too much borne in mind by most physicians. The patients are sent each year for some weeks to Carlsbad, Neuenahr, or Vichy. There all goes well, because the diet is properly controlled, not because of the waters; these have hardly any effect on the disease. But at home, the food is badly regulated; the effect of eleven months at home is naturally greater than that of one month at a health-resort; gradually, retrogression comes on, because over-loading the island-system is not avoided. I cast this reproach directly on the mineral-water treatment at well-known watering-places, that they create a false sense of security in the patients, who imagine that one month's treatment will do all that is necessary for themselves and their future. So unbounded is the faith in the "waters," and so great the suggestion which the *genius loci* exercises on both doctor and patient, that the best supported facts of modern metabolic theories are unable in any way to affect the old methods.

The more we have to insist, in accordance with the facts, upon treatment of the early stage, so much the more important becomes the early diagnosis of diabetes. In this connection, only the regular family doctors can bring about improvement, because they can make a point of testing their patients' urine for sugar, at least once a year. Testing the night-urine is not to the purpose, for that may be free of sugar, even in advanced cases of diabetes; whilst one or two hours after a meal rich in carbohydrates, from 1 to 2 per cent. of sugar is found in the urine. These tests should, therefore, always be made directly after taking a large quantity of carbohydrates. In convalescence after acute infectious fevers, the analyses must be made with special frequency in the months immediately following the attack.

THE INTERNAL SECRETIONS OF THE ALIMENTARY CANAL.

By W. LANGDON BROWN, M.A., M.D., F.R.C.P.

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UNTIL twelve years ago the alimentary canal was assumed to be outside the domain of the internal secretions. All its functions were regarded as under the control of the central or sympathetic nervous systems. Though Pawlow himself subscribed to this doctrine, the revision of the physiology of digestion which resulted from his work has led to the recognition of some undoubted and striking examples of internal secretions in the digestive area. *A priori* this might have been anticipated if it had been realized that while the assimilation of food is a primary need of every organism, however lowly, the development of a nervous system is a comparatively late event in evolution. As Starling pointed out, the nervous system enables very rapid reactions to occur, but where less sudden responses are needed, the primitive method is retained.

Thus salivary secretion may occur before the food enters the mouth; and though gastric secretion is started by the appetite and the taste of the food, it is continued by chemical stimuli, while pancreatic secretion can be explained by chemical factors alone. As the need for rapidity of response grows less, there is a gradual transition from a nervous to a chemical mechanism, which latter depends on hormones formed within the glands of the alimentary tract.

THE STOMACH.

It is in strict accord with this general statement that careful experiment has failed to detect any hormone formed by the salivary glands. In the stomach, however, the case is different. There is a striking difference between the histological structure of the glands of the fundus and the

pyloric portion. In the former the glands are narrow-mouthed, unbranched and composed of two different types of cells. The chief cells, lining the lumen, contain granules of pepsinogen, while external to these are ovoid cells secreting the hydrochloric acid. The pyloric glands, on the other hand, are wide-mouthed, branching and non-granular. It might be expected that such different glands would have different functions, but this was not realized until Edkins applied Bayliss' and Starling's experiments to the stomach. He made an extract of the pyloric mucous membrane of a cat's stomach with 0·4 per cent. HCl, and injected this into the circulation of another fasting animal. A secretion of gastric juice, containing both hydrochloric acid and pepsin followed. Extracts made with boiling water, glucose, glycerin or peptone produced similar though less marked effects. Meat extracts containing kreatin, however, yielded even better results than those made with hydrochloric acid. Similar extracts made from the glands of the fundus caused no secretion.

If the stomach were divided into fundus and pyloric portions by a tampon, the injection of pyloric extracts into the circulation caused gastric juice to appear on the fundus side, but not on the pyloric side of the division. The conclusion is inevitable that the substances mentioned stimulated in the pyloric mucosa the formation of a *gastric secretin*, or gastrin, which passing by the blood stream excited the secretion of gastric juice by the fundus glands.

As the food passes over into the pyloric portion, it can be sent on into the duodenum, if it be already sufficiently digested, but otherwise it is kept in contact with the pyloric glands, where it evokes renewed secretion from the fundus glands to complete its digestion. With this is probably related the comparative absence of peristaltic waves in the fundus, unless there is obstruction to the outlet, whereas, movements in the pyloric half are powerful and obvious on X-ray examination. It would only be reasonable, indeed, to expect that there must be some additional stimulant to gastric secretion besides the appetite and sense of taste. Otherwise it is difficult to see how digestion would be completed when once the sense of taste was in abeyance and hunger was assuaged. The importance of this mechanism is seen in

disease. In hyperchlorhydria, there is pyloric spasm which must result in keeping the food longer than usual in contact with the pyloric glands. Thus, the secretion of still more acid is excited and a vicious circle is established. In new growth of the stomach, on the other hand, there is usually no free hydrochloric acid and very little physiologically active HCl. Yet the pyloric portion of the stomach is far more commonly the seat of growth than the portion of the stomach which secretes the acid. No doubt to a considerable extent the low acidity is due to neutralization by the alkaline secretion of the growth; but I have repeatedly found, by test meals, that the total output of chloride has been diminished, so that it is in such cases, not merely a question of neutralization but of diminished secretion. My suggestion is that this is accounted for by the destruction of pyloric glands in which the normal stimulant to continued gastric secretion is formed.

If we consider the functions performed by hydrochloric acid, it will be clear that, in its absence, digestion cannot be performed satisfactorily, nor if it is in excess, will the patient be free from symptoms. The hydrochloric acid in gastric juice has to (1) render the pepsin active; (2) act as an antiseptic; (3) hydrolyse cane-sugar; (4) regulate the opening of the pyloric sphincter; (5) act as a stimulant to the secretion of the pancreas.

In the absence of hydrochloric acid, peptic digestion cannot be performed, micro-organisms of various kinds can flourish in the stomach and cane-sugar, not being inverted will excite a secretion of mucin. All this occurs in new growth of the stomach, in achylia gastrica, and in chronic gastritis. While in the stomach, the acid tends to open the pyloric sphincter, but, as soon as it passes into the duodenum, it brings about a reflex closure of the orifice. Therefore, either defect or excess of acid interferes with the due emptying of the stomach. If it is in defect, the pylorus remains unopened and the gastric contents are retained and continue to ferment; if it is in excess, each wave of the highly acid chyme into the duodenum produces pyloric spasm until the alkaline pancreatic juice has been able to neutralize this acid and thus relax the spasm.

Applying these facts to treatment, we have to regulate

the intake of those substances which are known to excite a secretion of acid. Nevertheless, we cannot be sure that they will act as in the normal stomach because the pyloric glands may be incapable of performing their work. It is generally agreed that the following substances definitely stimulate the formation of gastric secretion in the pyloric glands. Meat extractives, such as are contained in soups, broths, and beef tea; alcoholic and aerated fluids, spices, mustard, pepper, salt, cloves, and tea. Coffee is more variable in its action. A cigar after meals stimulates secretion in an habitual smoker. It follows that meat extracts of all sorts should be forbidden in hyperchlorhydria, though this does not mean that meat itself must be forbidden since it is not a mere stimulant, but provides some protein on which the gastric juice can act. The other stimulant substances should be regulated and diminished according to the needs of the case. In several instances I have found the restriction of salt a very useful procedure.

The late Sir Andrew Clark was accustomed to forbid his dyspeptic patients soup on the grounds that it diluted the gastric juice. This is apparently not the correct explanation of the beneficial effects which undoubtedly often follow that restriction. Presumably, the success occurred in the hyperchlorhydric cases, for, in the ordinary way, soup is a suitable beginning to a meal, the warm fluid causing vaso-dilatation and containing a stimulant to the gastric juice while not, in itself, taxing the digestive organs. In the opposite condition of absent or diminished hydrochloric acid, meat extracts are indicated, but should not be given in too much fluid because of the tendency to atonic dilatation to which such cases are always prone. Therefore, a little quite strong soup or broth, say, not more than five ounces at a time, is better than a larger quantity of a more dilute soup.

The medicinal regulation of hyperchlorhydria and achlorhydria lies outside the scope of this paper.

THE DUODENUM.

As soon as the acid chyme enters the duodenum, the secretion of pancreatic juice begins. It was at first thought by Pawlow that the acid chyme stimulated special nerve endings

in the duodenum, but Wertheimer showed that the acid was just as effective after all the nerves in the neighbourhood had been divided. The lower down in the intestine the acid was introduced, the less effect it produced until, at about two feet above the ileo-cœcal valve, it ceased to have any action at all. Further, if acid were introduced into the blood stream, it had no effect. This suggests that the acid acts upon something in the mucosa of the intestine, as was proved by Bayliss and Starling's classical experiment. A saline extract of the intestinal mucosa was treated with hydrochloric acid and injected into the blood stream. This produced an immediate and more marked secretion of pancreatic juice than could be achieved in any other way. Evidently, the acid excites the formation in the intestinal mucosa of some substance which is carried by the blood stream to the pancreas stimulating it in its turn to secretion.

The name "prosecretin" has been given to the precursor found in the mucous membrane and "secretin" to the substance resulting from the action of the acid upon it. These observations have been confirmed by all those investigators who have adopted a satisfactory technique. In this way, the existence of a hormone formed in the alimentary tract was definitely established for the first time. Secretin corresponds to other hormones in being a substance of small molecular weight and in not being a ferment. In spite of much research, however, its actual chemical composition remains unknown. It appears to stimulate the formation of all the ferments of the pancreatic juice. It is, therefore, difficult to believe that modifications in the diet can alter the composition of pancreatic juice as was claimed by Pawlow and, subsequently, by Bainbridge. According to the latter, a special ferment, lactase, could be produced in the pancreatic juice by keeping adult animals on a milk diet. It was a tempting hypothesis, suggesting that if only Nebuchadnezzar had persisted in his attempts to eat grass like an ox, he would ultimately have been able to digest it like that animal. Later observations have, however, completely disproved this theory of the adaptability of the pancreatic secretion.

Practical applications of secretin in treatment have not yet been successfully made. In the first place, secretin as

such cannot be absorbed from the alimentary tract; it must be made within the intestinal mucosa; oral administration is therefore useless. In the second place, if injected into the blood stream, certainly it causes a rapid secretion, but if there is no food in the duodenum, a dangerous self-digestion of the walls takes place accompanied by an intense enteritis. It will be noted that, in the ordinary way, the alkaline pancreatic juice is never secreted until acid chyme enters the duodenum, and, moreover, should this accidentally occur, the trypsin does not become activated until it meets the succus entericus of the small intestine, which also depends on the presence of food for its appearance. At present our control over secretin is limited to regulating it through the acidity of the gastric juice. If there is inadequate gastric secretion, there will be inadequate pancreatic secretion. This can be rectified to some extent by the administration of acids or, better, acidol (betain chloride), which liberates nascent hydrochloric acid when freshly dissolved. Hyperchlorhydria, on the other hand, will tend to exhaustion of the pancreas and, therefore, should be controlled by suitable administration of alkali. It should be noted, also, that pancreatic inadequacy must tend to excite some degree of hyperchlorhydria, since the normal neutralizing mechanism is partially in abeyance. Here again a vicious circle becomes established which we can break to some extent by alkaline treatment.

Whether secretin is a stimulant of the internal as well as the external secretion of the pancreas is doubtful. Some observations suggested that in diabetes there was an absence of prosecretin in the intestinal mucosa, but Bainbridge found abundant prosecretin in a case of diabetic coma under my care, and this has been confirmed in many other cases. It is not surprising, therefore, to find that secretin, whether given by the mouth or hypodermically, has had no beneficial effect in diabetes; indeed, Tirard has found that trypsogen—a proprietary preparation of this kind—actually aggravated the glycosuria in the cases in which he tried it.

Secretin also causes a slight secretion of bile which might perhaps be expected, considering the close co-operation of the liver and pancreas in digestion. It has not proved of

any practical value, however, as a cholagogue.

The important subject of the internal secretion of the pancreas in relation to glycosuria is the subject of a separate article in this Special Number of THE PRACTITIONER and will not be dealt with here.

THE INTESTINES.

Very little definite evidence is available as to the formation of internal secretions by the rest of the alimentary tract. The mechanism of the secretion of succus entericus is still doubtful. According to Pawlow, it depends upon two factors, the mechanical distention of the bowel and the presence of pancreatic juice. Bayliss and Starling considered that the pancreatic juice acted upon the intestinal glands. Frouin thought, on the other hand, that succus entericus was its own hormone, so to speak, for if injected intravenously it produced an abundant secretion. He suggested that some ingredient of this juice acted as a stimulant to the secretion of fresh succus entericus in the next loop of the bowel. The nature of the active ingredient is unknown. Attempts have been made to base a treatment for constipation upon this, but it is too early to express any definite opinion as to its value. Succus entericus contains several ferments—(1) enterokinase, which activates the trypsinogen of the pancreatic juice; (2) erepsin, which completes the digestion of ordinary protein and can, by itself, digest casein and gelatine; and (3) sugar-splitting ferments, such as invertase for cane-sugar, maltase and lactase. Such digestion of cellulose as is accomplished is probably carried out by bacteria and by ferments contained in the vegetable food itself. In this way, digestion is continued in the cæcum of the herbivora, in which animals this part may attain a great size, exceeding that of the stomach.

Much speculation has been indulged in as to an internal secretion formed by the appendix and, therefore, presumably, by other collections of lymphatic tissue in the bowel such as the Peyer's patches. But there is no direct evidence of anything of the kind; in fact, lymphatic tissue throughout the body does not appear to form any hormone, but is con-

cerned with absorption, filtration and the manufacture of lymphocytes.

THE LIVER.

For a long time, the discrepancy between the size of the liver and the meagre amount of its external secretion, the bile, was a puzzle to physiologists. Gradually it was realized that the organ had important duties in the metabolism of all the three foodstuffs and work in connection with hæmolysis and coagulation as well as antitoxic functions. In connection with all of these, substances are undoubtedly poured into the blood-stream by way of the hepatic vein, but it is doubtful if any of them really come within Starling's definition of a hormone, a chemical messenger which, carried by the blood-stream, excites some other gland into activity. Rather have these substances been prepared for assimilation by the tissues or transformed into an inert and convenient state for excretion. A brief summary of these various functions will enable the reader to decide for himself how far their performance involves a true internal secretion.

(1) *In connection with Nitrogenous Metabolism.*—That the liver is the principal though probably not the only seat of the formation of urea, has been known for a long line. But at first it was regarded mainly as the place where the ammonium salts derived from the breaking down of tissue proteins underwent their final transformation into urea. To-day we know that the greater part of the urea is formed directly from the food and that the products of protein digestion are thrown into the portal circulation mainly, if not entirely, as simple amino-acids. From these, the liver apparently selects those which are needed for the immediate nutrition of the tissues, and it deprives the remainder of their amine groups, converting them into urea. The carbonaceous residues we may presume are utilized as an immediate source of energy.

But urea is not formed simply from protein. It is now realized that a large quantity of the ingested purins are rapidly destroyed in the liver to form urea by way of allantoin. The proportion thus dealt with varies with the different purins; of some only one-half is converted, and of others, as much as nine-tenths. The recognition of this capacity of the liver to deal with the purins of the food was the death-blow to the con-

ception of gout as a food poisoning. In this theory lay implicit the idea that the body could deal with the purins formed in the tissues (the endogenous), while unable to dispose of the purins of the food (the exogenous). The reverse of this would appear to be the truth, and gout now appears to be far more a symptom of failure to metabolize purins than a poisoning by the purins of the food.

The liver destroys purins by means of intra-cellular ferments such as uricase and xanthase. This by no means exhausts the list of its intra-cellular ferments. It is probable that all the different amine groups derived from proteins require their own special ferments, and Garrod in his classical work on the inborn errors of metabolism has been able to demonstrate the existence of some of them. Thus, alkaptonuria is due to the failure of the liver to deal with the tyrosin of the protein molecule, so that an intermediate product, homogentisic acid, appears in the urine, imparting a brown colour to it on standing or on making it alkaline. Further, the urine is now capable of reducing Fehling's solution, so that some of the sufferers from this harmless inborn error have been labelled as diabetics. It is perhaps going too far to regard the condition as entirely harmless, since it leads to that disfiguring deposit of pigment in the conjunctiva, ear-cartilages and elsewhere, called ochronosis. It also appears to be associated sometimes with a special form of chronic arthritis producing a curious "goose-gait."

Cystinuria again is due to the absence from the liver of an intra-cellular ferment which should break down the sulphur-containing fatty acids in the protein molecule. This causes no symptoms beyond the deposit of cystin crystals in the urine unless an infection of the urinary tract occurs, when cystin calculi may form. It is curious that this incapacity for dealing with cystin should relate only to that formed by the tissues, for, if a sufferer from this condition is given some of his own cystin by the mouth, he is able to deal with it satisfactorily. It is highly probable that further research will demonstrate the existence of many other such intra-cellular ferments in the liver and that we may look forward to the time when, as Hopkins puts it, we shall speak of a man, not as possessing a diathesis, but as lacking an

intra-cellular ferment.

(2) *In connection with Carbohydrate Metabolism.*—Ever since the days of Claude Bernard, it has been realized that the liver was an important storehouse of carbohydrate in the form of glycogen. This subject, however, is closely associated with glycosuria and the internal secretion of the pancreas, and is dealt with fully in the article on that organ. It will be sufficient here to point out that the ultimate product of this function passes into the portal vein as dextrose, which does not come within the definition of a hormone even though its formation may depend on a hepatic intra-cellular ferment.

(3) *In connection with Fat Metabolism.*—Leathes has shown that the fat normally present in the liver is in the more active, unsaturated form, but that the fatty deposit which occurs there in poisoning by phosphorus or after anæsthetics is in the more inert, saturated form. He makes out a good case for regarding as a function of the liver the conversion of fat into the more active unsaturated form for utilization by the tissues. When the liver is thrown out of gear by various toxins, of which we have mentioned the most important, the tissues, starving for prepared fats, send unprepared fats to the liver, but in vain, for it is unable to deal with them. The liver may be compared to a miller ; the saturated fats are the wheat he grinds and the unsaturated fats are the flour that results. It will be noted, however, that throughout this process, although there is transference of nutritive material, there is no evidence of the entrance of a chemical stimulant or messenger into the blood-stream.

(4) *The Anti-toxic Functions of the Liver.*—Amid the stream of substances passing from the intestines by the portal vein to the liver, some might be expected to be toxic. Eck's fistula, a communication between the portal vein and the inferior vena cava, is followed by toxic symptoms. Some of these, no doubt, are due to the presence of unprepared and excessive amounts of amino-acids, but others are probably due to products of intestinal putrefaction. Some, at least, of the latter are known and have been isolated. Thus, the tryptophan of the protein molecule is split by intestinal bacteria into indol and skatol. As shown by Herter, indol is mildly toxic. It is not excreted as such in the urine but as indican, a harmless compound of

indol with a sulphate. This combination is apparently effected in the liver. Occasionally, a less completely neutralized body, indol-acetic acid, may escape into the urine; I have then generally found definite evidence of toxic symptoms.

Indican is by no means the only one of these compound or ethereal sulphates to be formed, but owing to the striking reaction it gives, it is the one which has attracted most attention. If a little urine is mixed with an equal quantity of strong hydrochloric acid, and two or three drops of hydrogen peroxide added, a blue colour is imparted to chloroform shaken up with the contents of the test-tube. This is the simplest and most sensitive test for indican; indol-acetic acid gives a bright red colour with this test. It is important that the urine should be tested fresh, for indican tends to disappear on standing. Indican is normally absent from the urine of infants and children because, in them, intestinal putrefaction is at a minimum. As life goes on it tends to appear, especially in those of a sedentary habit. Excessive indicanuria probably means exaggerated intestinal putrefaction, but a moderate amount is compatible with good health, though, as Herter puts it, its absence implies that the individual is a candidate for old age. I have said that indican is not the only ethereal sulphate in the urine; unfortunately it does not bear any constant relation to the total amount of them. Thus, I have had cases with a small amount of indicanuria, although the total quantity of ethereal sulphates was high; according to Mackenzie Wallis, this is typical of colitis. But, at any rate, indican provides us with a good example of the anti-toxic action of the liver, or, as it has been called, a negative internal secretion.

Glycuronic acid is another protective substance formed by the liver. It differs chemically from dextrose only in having an acid group in place of an alcohol group, but, like it, can reduce Fehling's solution, though it does not ferment, and forms different crystals with phenyl hydrazine. It usually appears in the urine as the result of the administration of chloral, camphor and opium, or its derivatives. These substances are partly voided as compound glycuronates whose formation is carried out by the liver. Here again we have an antitoxic mechanism. It is possible that glycuronic acid is formed from the glycogen there, for the chemical relationship is a near one, and the liver

appears to be able to perform its anti-toxic functions better in the presence of glycogen.

This reaction to an administered drug may cause confusion when that drug is codeia given for glycosuria. I recently saw a patient who had been glycosuric, and whose urine, despite diet, still contained a small amount of reducing substance. The reduction did not seem to me to be like that of dextrose, however, and on further analysis, I was able to show that it was due to glycuronic acid. It occurred to me that this glycuronic acid was probably due to the codeia, and I accordingly advised its discontinuance. This was followed by the disappearance of any reduction, which was therefore due to the drug. The significance of this is clear, and I would urge that, in any case, it is unnecessary to give codeia for a trace of sugar in the urine. Its use should be confined to cases in which the output of sugar is large in spite of careful dieting. The formation of glycuronic acid by the liver can probably be excited by other substances than administered drugs, and it provides another interesting example of negative internal secretion by the liver.

In addition to these inherent anti-toxic powers, the liver seems to be able to acquire others. Thus Emerson Lee believes that tolerance to tobacco is acquired by the formation of a nicotine-destroying ferment in the liver.

Of the other liver functions, our knowledge of those in connection with the coagulability of the blood are at present too vague to throw light on this topic, while those in connection with hæmolysis relate solely to its external secretion, the bile.

Considering these manifold functions of the liver, it would not be surprising that a very slight upset of them should produce toxic symptoms. "Biliousness is a very common state, a very real state, but one that is very little understood," and I would suggest that it is often due to an infection of intoxication of the liver resulting from the activities of B. coli. During cyclical vomiting in children, which is closely related to bilious attacks in older persons, B. coli may often be found in the urine, and in both conditions the agglutinating power of the patient's blood against B. coli may be found to be increased. In eclampsia and in acute yellow atrophy of the liver, we meet with a much more profound, though similar

toxæmia, associated with organic changes in the organ.

Reviewing the whole evidence it would appear that the only two proved examples of hormones formed within the alimentary tract are gastric secretin and the secretin formed by the duodenum and, to a less extent, by the rest of the small intestine. One of its annexes, the pancreas, forms a hormone concerned with carbohydrate metabolism, while another, the liver, although forming many intracellular ferments and several antitoxic substances, does not appear to form hormones in the strict sense of the word.

THE USE OF HORMONES IN MEDICINE.

By GEORGE R. MURRAY, M.A., M.D., D.C.L., F.R.C.P.

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During recent years, much light has been thrown upon the mode of action of the internal secretions. It has been shown that they owe their properties to certain bodies, which have a remarkable power of stimulating activity in cells situated at a distance from the secretory gland itself. These bodies have been appropriately named "hormones" by Professor Starling. Some certainly are "awakeners" of metabolic activity, but others, for which the name "chalones" has been suggested by Sir E. A. Schäfer, probably exercise a controlling or inhibitory effect on certain forms of cellular function.

Starling has divided the hormones into two classes, the acute and the chronic, according as the results of their action are immediately or more remotely apparent. Adrenalin furnishes a good example of a hormone which may have an acute or immediate effect. It has been shown clearly by the investigations of T. R. Elliott, B. Cannon, and others, that under the influence of a strong stimulus, such as is furnished by fright, adrenalin is rapidly discharged into the adrenal veins and so into the general circulation. It is interesting to follow up the effects of this condition of adrenalinæmia, and to see how useful they may be to an animal either in contending with or escaping from the cause of its fear. The excess of adrenalin dilates the coronary arteries giving the heart a larger supply of blood, increases the strength of the cardiac contractions, and raises the blood-pressure. It tends to divert the chief flow of blood from the abdominal vessels to those of the central nervous system, heart, lungs, and muscles. The adrenalin thus stimulates just those activities, which an animal chiefly employs in either fighting a foe or escaping from an enemy. In addition to this, the adrenalin mobilizes the store of glycogen in the liver, thus increasing the amount of sugar in the blood and rendering it available for use in the muscular

exertion entailed by the effort.

The chronic class includes hormones like those supplied by the thyroid gland. Their action on metabolism, general nutrition and the nervous system is continuous, and does not produce immediate or sudden effects.

It will be convenient to consider the uses of these two classes of hormones in medicine separately. The hormones of the acute class are available to produce rapid and immediate results, but their action is short in duration. Those of the chronic class, on the other hand, produce no apparent effect until some time has elapsed, but by appropriate spacing of the doses their action may be kept up continuously for as long as necessary, even for a whole lifetime. Adrenalin is probably passing continuously into the blood stream from the medullary portion of the gland in very minute quantities, but, as we have seen, on occasion the supply can suddenly be increased, until the emergency is passed. When applied locally in the strength of a 1 : 1000 solution, adrenalin chloride has powerful vaso-constrictor action. It is thus very useful in arresting hæmorrhage from superficial cuts and abrasions. This action is readily visible, if a piece of lint, moistened with a few drops of the solution, is firmly applied to an abrasion of the skin for a minute or two. The hæmorrhage ceases, and the skin for a short distance round becomes pale. It may be used in a similar manner for the arrest of epistaxis.

In cases of hæmatemesis, the same solution may be given in ten to fifteen minim doses, every 2 hours. In cases of hæmorrhage from piles, it may be employed in a suppository. On account of the vaso-constrictor action, adrenalin is largely used in combination with local anæsthetics, as it limits their area of action and diminishes absorption, so that a smaller quantity of the anæsthetic is required. It is doubtful whether adrenalin, when taken by the mouth, has any action beyond that of causing contraction of the vessels supplying the mucous membrane of the stomach; the question will be considered later, in connection with the chronic action of hormones.

Adrenalin may be given, by hypodermic injection, most conveniently in the form of the 1 : 1000 solution of adrenalin chloride in doses of from one to five minims. In this way, its normal action already described may rapidly be obtained.

Caution, however, is required in the use of a remedy with such powerful physiological action. Patients differ considerably in their susceptibility, so that, in the first instance, it is advisable to give not more than one or two minims. Dr. Miller[1] has found that the initial effect may be to cause a sense of oppression or even faintness, with acceleration of the pulse to 110, or even 130, and marked pallor. These symptoms pass off in the course of a few minutes; the pulse then becomes steady, of good volume, and slower by some ten beats a minute than it was before, and this effect is maintained for several hours.

If by chance the injection is given into a vein, an alarming condition of collapse may follow, though I do not know of any case in which the result has been fatal. In the treatment of asthma, adrenalin is of great service in relieving the actual attacks. The effect, however, is temporary and it does not appear to diminish the tendency to the attacks. It has been shown by Dr. Hertz that prompt relief may be obtained by the injection of as little as one minim of the 1 : 1000 solution, so that this dose should always be tried in the first instance. If it is found to be insufficient, the dose may be increased up to three or five minims. In a very severe case of asthma, under my care at the Manchester Royal Infirmary, this was the only remedy which gave relief. If necessary, the injection can be repeated twice or thrice in the twenty-four hours.

Adrenalin has been largely used in the treatment of shock. This condition is due to exhaustion of the vaso-motor centres, in consequence of which the blood-pressure becomes dangerously low, it may fall to 50 mm. of Hg. or lower. Adrenalin is useful in raising the pressure, and so helping to maintain the circulation until the nerve-centres recover. It has been given per rectum in the proportion of one drachm to a pint of normal saline solution. Mr. P. Lockhart Mummery,[2] however, states that it must be given intravenously because rectal or subcutaneous injections are useless. For intravenous injection, the adrenalin should be added to the infusion fluid, in the proportion of 1 to 30,000, and the fluid run in until the blood-pressure rises to 130 mm. of Hg. After this, the blood-pressure can be maintained by running in the fluid very

[1] *Lancet*, July 18, 1914, p. 158.
[2] A System of Treatment, Vol. I., p. 102.

slowly at the rate of two or three minims a minute. In cholera, adrenalin has proved to be of service, and may be administered in the same manner as in the treatment of shock.

Of late, adrenalin has been used as a test for pancreatic insufficiency. Loewi's test, as it is called, is carried out by instilling one or two drops of adrenalin chloride solution into one eye. Care must be taken to see that the eye is healthy, and that there is no lesion of the conjunctiva. In cases of pancreatic disease, the pupil dilates within half an hour. This test is of considerable service, when taken with the other factors in the case. Dr. A. E. Garrod has found the test positive in all pancreatic cases, and very rarely in other diseases. It has been stated that the reaction is positive in Graves's disease. I have, however, not yet seen dilatation of the pupil in any of the limited number of cases of this malady, in which the test has been applied. In one of the cases in which it was negative, the sugar-tolerance was diminished, for glycosuria followed a single dose of 100 grammes of glucose. The test was also negative in a case of acromegaly with glycosuria, which was under my care in the Manchester Royal Infirmary. The test is probably a valuable addition to our methods of examining cases of suspected pancreatic disease, though we are not yet in a position to estimate its exact value.

There are certain conditions under which the use of adrenalin is contra-indicated. Arterio-sclerosis has been produced experimentally in animals by the continued use of adrenalin. This is not likely to occur, when it is used for its immediate effects alone and for a short period. Bearing in mind its physiological properties, however, it is evident that adrenalin should not be employed in cases of arterio-sclerosis, nor in any patients with an abnormally high blood pressure. It should not be used in any case of hæmoptysis, nor in any case in which glycosuria is present.

PITUITARY EXTRACT.

The pituitary hormones probably differ in action according to whether they are derived from the anterior or posterior lobes of the gland. The hormones supplied by the posterior lobe and *pars intermedia* belong to the "acute" class, and can

be used in medicine to produce their effects rapidly. These hormones have been shown by Sir E. A. Schäfer to control the contractility and tone of plain muscular fibres. They stimulate the constrictor muscles of the arteries, uterus, bladder, and intestine, and they increase the secretion of the kidney and mammary gland. The extract is available under the name of "pituitrin," "hypophysin," or "infundibulin." A single hormone, hypophysin, has been isolated, and employed as hypophysin sulphate in a 1 in 1,000 solution. The ordinary extracts, however, probably contain several hormones, and Führer has found four different substances which are active.

Pituitary extract is specially useful in the treatment of shock, as was shown by Blair Bell. Of late, it has largely taken the place of adrenalin, because its action in raising blood pressure is equally prompt, but instead of the effect passing off in a few minutes, it is maintained for half an hour to an hour. Like adrenalin, it should be injected into a vein. The dose of the extract is from seven to fifteen minims. This dose may be repeated several times if necessary, at intervals of an hour or two. Hypodermic injections also have a useful effect, but are less efficient in the treatment of shock; they have, however, been used with advantage in pneumonia, as soon as signs of cardiac failure appear. Owing to the direct action of the pituitary hormones on the muscular walls of the intestine, the extract is useful in tympanites and post-operative distension, for it enables the muscular fibres to regain their normal tone, and it stimulates peristalsis.

The action upon the uterus has led to its extended use in obstetric practice, both to stimulate contractions in an atonic uterus, and in the arrest of post-partum hæmorrhage. In the latter, it is said to increase the action of ergot, so that a powerful effect may be obtained by a combination of the two remedies. Pituitrin may be injected into the muscles in doses of seven to fifteen minims, when it is desirable to obtain a prompt action on the bowel or uterus. Pituitary extract has a distinct diuretic action, but it has not been much employed for this purpose, and therefore no clear indications can be given for its use. Uræmia is said to be favourably influenced by intravenous injection of 1 cc. of the extract in a pint of normal saline solution.

During lactation, pituitary extract produces a striking

increase in the flow of milk for some 10 or 15 minutes. It is, however, still doubtful whether the total secretion in 24 hours is really increased in amount under its influence.

In the persistent vomiting, which occurs during a gastric crisis in Graves's disease, pituitary extract is sometimes of great value. In one case I have seen, the injections of pituitary extract effectually controlled the vomiting, which finally ceased altogether; in another, they controlled the vomiting on one occasion, but later on they lost their effect.

SECRETIN.

One of the most typical examples of acute hormone action is furnished by secretin, originally discovered by Professor Starling. This hormone is set free in the cells of the mucous membrane of the duodenum, as soon as the acid chyme from the stomach passes into it. The secretin is carried by the blood to the pancreas, in which it stimulates secretion. It is unfortunately difficult to make use of this hormone in medicine, for Starling has shown that it is destroyed when given by the mouth. Its physiological effects can only be obtained by injection into the blood, which is not a practical method for the frequent repetition required in the treatment of conditions of pancreatic insufficiency.

The use of duodenal extracts containing secretin has been carried out by Harrower, and the clinical results have indicated that the preparation is not inert. It is evident that further investigations are necessary, before any conclusion can be drawn as to the therapeutic value of this extract. The dry duodenal extract may be given in doses of one to three grains, repeated every 20 minutes for an hour, or even longer.

Of the *chronic hormones*, those supplied by the thyroid gland furnish the most typical example. Fortunately, these hormones can easily be obtained, and they are absorbed from the alimentary canal without losing their physiological properties. In either liquid or dry thyroid extract we can readily administer the thyroidal hormones by the mouth, in suitable doses, to replace the function of a thyroid gland which has atrophied. This supplemental treatment is employed to the greatest advantage in myxœdema and cretinism. The details of this treatment, and the precautions which must be taken, hav already been described so fully elsewhere that it is

only necessary to mention one or two points here. It is important to remember that cases of myxœdema and cretinism occur in all grades of severity, from those in which the thyroidal insufficiency is only slight and the symptoms are mild, to those in which the thyroid is almost, if not quite, functionless, and the symptoms present a typical clinical picture which is recognizable at a glance. It is important to recognize these slight cases, for prolonged ill-health may be the result of overlooking their true character. If there is a doubt, a course of treatment by small doses of thyroid extract, *e.g.*, liq. thyroidei ♏ v., or one or two 2½ grain tablets a day, will soon be followed by improvement, if the thyroid is at fault. In the systematic treatment of myxœdema and cretinism, it is advisable to explain to a patient the nature of the treatment and, as it is supplemental, the necessity of its continuance for the rest of life. It is also important to select a preparation of known activity.

When the secreting tissue of the thyroid has largely been destroyed and the symptoms are well marked, it is usually necessary to work gradually up to a nightly dose of liq. thyroidei ♏ x. or one five-grain tablet. In a few cases, half as much again, or even twice as much, has been found necessary to keep up an adequate supply of the thyroidal hormones and maintain the patient in a condition of health.

Thyroid extract is serviceable in the treatment of the simple parenchymatous goitre of puberty and adolescence. A single dose of from two to five grains of dry thyroid, each night at bed-time, is often followed by a gradual diminution in the size of gland. This is probably due to the natural call for increased internal secretion, at this time of life, being met by the supply from an external source. Further, we may employ the thyroidal hormones in cases in which there is no evidence of thyroidal insufficiency, when their physiological action may serve a useful purpose. This is notably the case in the treatment of some chronic diseases of the skin, such as psoriasis, and in the treatment of obesity combined with a suitable dietary. In some other diseases, such as rickets and rheumatoid arthritis, the favourable results which have been obtained by some observers may be due simply to the iodine contained in thyroid extract, and not to the physiological action of the thyroidal homones.

In Addison's disease, which is due to destructive disease of the suprarenal glands, there is loss of adrenalin; but this is not all, and it is probable that the cortex of the suprarenal gland supplies a hormone of the chronic class to the loss of which some of the symptoms are due. This has not yet been proved, and no constant results have been obtained in the treatment of this disease by any form of suprarenal extract. In a few cases, good results have been recorded, but the general experience, with which my own agrees, has been unfavourable. The late Dr. G. Gibson recorded very good results from the employment of suprarenal extract in Graves's disease. After an extensive trial, I am unable to support his opinion of its value, though it has appeared to be of service in some cases. The failure of suprarenal extract in Addison's disease may be due to either loss of activity of the hormones or to lack of absorption from the alimentary canal.

PITUITARY EXTRACT.

It is probable that the anterior lobe of the pituitary gland furnishes a hormone of the chronic class, the excessive secretion of which brings about the hypertrophic changes which occur in acromegaly. When this hormone is lacking, the interesting but rare condition of adiposo-genital dystrophy develops. In the later stages of acromegaly, there is not infrequently a condition of pituitary insufficiency as well. Under these circumstances, it has been shown by H. Cushing that treatment by pituitary hormones is of value. Large doses, however, appear to be required, as 12 grains of the dried whole gland preparation were given three times a day in one case, and as much as 300 grains a day in another.

There are other hormones which may ultimately prove to be of permanent value in medicine, but on the present occasion we are chiefly concerned with those which have proved to be of real value in the treatment of disease. Hormones which are formed by the pancreas, testis, ovary, and other organs play an important part in maintaining a normal condition of health, but there is still reason to doubt whether the ordinary extracts of these glands contain them in an active form. Further investigation is required to show whether in the present form they possess any real value as therapeutic agents or not.

THE USE OF HORMONES IN GYNÆCOLOGICAL AND OBSTETRICAL DISORDERS.

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ALTHOUGH for many years I have investigated, experimentally and clinically, the relation of the internal secretions to the special functions of the female in health and disease, I was somewhat taken aback when asked by the Controlling Editor of THE PRACTITIONER to contribute to this Special Number. I had the uncomfortable feeling that I was being invited to stand and declare. This spontaneous attitude of mind expresses, and its exposure emphasizes, more forcibly than anything else how difficult it is to put into definite words, without a mass of supporting scientific evidence, any knowledge I may have of this complex subject, so that it may be lucid to all. Yet, I believe, that the time has come when attempts should be made to formulate our position from a clinical and therapeutical standpoint, if further headway is to be made in this vast but roughly outlined field of biochemical medicine.

It can only be a matter of time before what are now described in general terms as the characteristics and effects of the internal secretions will be discussed in the terms of biochemical details, both in the cause and effect. This scientific era in the study of the hormones cannot be long delayed, for from a sporadic interest spread over several decades universal concentration of our scientific forces, in the laboratory and at the bedside, is being directed towards this all-important subject. In saying this, I do not think I am exaggerating the importance of the "Regulators of metabolism," as they have aptly been called by Professor Noel Paton in his highly suggestive work on this subject.

There is, however, much of extreme physiological and

pathological interest in regard to the relations of the internal secretions to the normal and abnormal specialized functions of the female which will not come under consideration here. I am not concerned now with the normal functions, nor shall I attempt to discuss those anomalies of which either we know little or are unable specifically to deal with in practice. I have discussed these wider aspects of the subject elsewhere.[3, 5] Moreover, in the time and space at my disposal I shall only be able to take a brief and general survey of that specialized part, which falls to my lot, of the comprehensive subject of the internal secretions.

TREATMENT OF GYNÆCOLOGICAL DISORDERS.

The internal secretions regulate not only the formation of the genitalia, but also their subsequent and complete development. That is to say, there are two stages in the development of the normal genitalia: the primary or fœtal, and the secondary or pubescent. Further, during the reproductive life of the individual, the control of the normal functions is under the influence of the endocrinic organs; and finally, the menopause consists not merely of atrophy of the ovaries and the rest of the genitalia, but also of changes in the correlated organs of internal secretion.

It will be most practical, then, if we consider the hormone therapy of gynæcological disorders in their connection with these three subdivisions.

DERANGEMENTS OF PUBERTY.

Incomplete development.—Treatment can only be possible when the *secondary* development is at fault. In such circumstances, the development has presumably been normal in fœtal life and during childhood, but has become arrested or shown incomplete development by the time puberty is reached, and subsequently. Clinically, then, we may meet with cases of incomplete puberty; that is to say, all the characteristics of puberty are present except the appearance of menstruation. This condition may be produced, of course, by maldevelopment of the uterus in fœtal life and many constitutional diseases, but we shall only discuss those conditions in which hormone

therapy can be of value.

Cases of incomplete development which may be improved are those in which there is pituitary, thyroid, or ovarian insufficiency. Naturally, the first important matter is to decide which internal secretion is at fault, after we have excluded all other causes of incomplete puberty. Let me say at once that it is impossible, in the scope of this article, to discuss the biochemistry of the blood and urine, which may furnish important clues. There is, however, certain clinical evidence which may assist us greatly, and, indeed, furnish us with sufficient information. Nearly all the patients are adipose, whether the insufficiency arise in the thyroid, pituitary, or ovaries. If there be pituitary insufficiency the skin will be found to be soft and smooth; if there be thyroid insufficiency it is harsh and rough. With pituitary insufficiency, the blood pressure tends to be below 110 mm. Hg.; but with thyroid insufficiency it is usually normal (125 mm. Hg.), or slightly above normal.

Ovarian insufficiency we can ignore from a diagnostic point of view; and this is convenient as it is most difficult to demonstrate. Such a proceeding is scientifically justified by the knowledge that both thyroid and pituitary insufficiency induce ovarian insufficiency. When we have decided whether it be the thyroid or pituitary which is at fault, we should treat the case by the administration of pituitary extract (whole gland, gr. v. three times a day) or thyroid extract (dried gland, gr. i. or more every night) as the case may be, together with ovarian extract (gr. x. three times a day). It is, further, my opinion that ovarian extract is of little use when given alone, but that good results may be expected when it is combined with thyroid or pituitary extract, according to which is required. I believe that luteal extract possesses no advantage over whole-ovary extract; indeed, I prefer the latter on scientific grounds. In those cases in which an accurate diagnosis has been made, treatment should be persevered with for some years. Success, however, is only likely to be obtained when the patient is seen before the age of twenty years.

Since incomplete development is liable to be followed by scanty menstruation and the premature menopause, treatment may have to be continued throughout the reproductive life of the individual. On the other hand, there can be no doubt that

the development of the uterus and normal menstruation may supervene on an incomplete puberty treated by the methods described.

Menorrhagia.—This is a common disorder at puberty, and one that may be very serious; yet apparently great difficulty is experienced in treating it successfully. Many cases are due to imperfect harmony between the counterbalancing secretions of the endocritic organs. There is at puberty a readjustment in the control of the metabolism; and if, for instance, the ovarian secretion be in excess of the normal, then menorrhagia will ensue. Similarly hyperthyroidism—and by this we do not mean exophthalmic goitre—may also produce menorrhagia and too frequent menstruation. To counterbalance these excessive secretions, we should prescribe pituitary or suprarenal extract.

It must not be forgotten that there are many other causes of menorrhagia at puberty not connected *directly* with the endocrinic system, and that these must be carefully investigated before resort is made to hormone therapy. Some of these apparently independent causes, however, may be influenced by the administration of some hormone preparation, and, in these circumstances, it will be found that we are really producing a true physiological effect. For example, menorrhagia is often due to an insufficient calcium content in the blood. Sometimes, the administration of calcium lactate in large doses will cure the patient. More often, however, at this time of life the onset of menstruation not only leads to excretion of calcium in excess of the normal, but also appears to prevent its fixation in the tissues and maintenance at a high level in the blood. There is no doubt that this may be the result of hyperactivity of the ovaries and thyroid.[4] But the administration of suprarenal extract, or, better, pituitary extract, not only counteracts the activity of the endocrinic organs mentioned, but also keeps high the calcium content in the blood.[3]

Dysmenorrhœa.—This is occasionally primary, that is to say occurs at puberty. In such circumstances, it is practically always due to imperfect development of the uterus, with or without acute flexions. Menstruation is usually scanty. Such cases, as we have already seen, are best treated with thyroid,

or thyroid and ovarian extracts combined.

Pubescent psychoses and neuroses.—These conditions are often due to disorders of menstruation. There is either menorrhagia, amenorrhœa, or scanty menstruation. The treatment of the nervous disorders is largely dependent on the rectification of the menstrual derangement, which may be one of those we have just discussed.

DERANGEMENTS DURING THE REPRODUCTIVE PERIOD.

Some of the conditions described already as occurring at puberty may be continued into the reproductive period, as it is called, of the patient's life. If so, we can always learn from the history that the trouble has existed from puberty. I shall now, however, mention those disorders associated with the menstrual function which arise after puberty, or at any rate are not specially dependent on the onset of menstruation for their appearance.

Amenorrhœa and Scanty Menstruation.—Secondary amenorrhœa may be directly due to disturbances in the endocritic system. When there are alterations in the sex characteristics, there is always amenorrhœa; but such conditions I shall not discuss now as they hardly come within the range of hormone therapy in the present state of our knowledge. But in some of the minor disturbances of internal secretion we can effect definite results.

Hypothyroidism may supervene after previously normal activity, and produce amenorrhœa or scanty menstruation. This condition has been known to follow acute fevers. The patients suffer with the symptoms and signs already described, and can be treated with thyroid extract with complete confidence in the result. Apart from the minor forms of hypothyroidism, we may meet with myxœdema as a cause of amenorrhœa. I have known a patient suffering with this disease to be cured by the administration of thyroid gland, and subsequently to menstruate regularly and conceive, after having had amenorrhœa for several years.

Hypopituitarism may also occur, without the intermediate condition of acromegaly, which Cushing[9] thinks is usually followed by hypopituitarism. In the minor cases, in which there has never been a suspicion of acromegaly, good results

may follow the administration of whole-gland pituitary extract.

Menorrhagia.—This may be due to excessive secretion of the ovaries or thyroid. Hyperoöphorism with menorrhagia is seen in girls who are engaged to be married, and who enjoy restricted sexual stimulation. As a rule, no treatment is necessary. If it should be, calcium salts, with pituitary extract to maintain the calcium in the system as well as to antagonize the ovarian secretion, would be indicated. The same treatment is most beneficial for menorrhagia seen in women about 35 years of age who have never married.

In the early stages of exophthalmic goitre, we often meet with menorrhagia. This symptom, and the disease which causes it, may be checked by infundibulin administered intramuscularly.

Menorrhagia due to chronic subinvolution of the uterus is best treated with pituitary extract made from the posterior lobe (infundibulin). This may be administered by the mouth in doses of two grains twice a day. Apart from subinvolution, women sometimes suffer with loss of tone of the uterine muscle, which is always associated with menorrhagia. This condition, too, can be cured with pituitary extract.

Dysmenorrhœa may be due to the loss of tone in the uterine muscle, which, as we have just seen, leads to menorrhagia. Now, I have shown [2, 6] that, if the blood be poured too rapidly through the endometrium during menstruation, clotting may occur in the uterine cavity because the fibrin ferment is not destroyed in the normal way. The expulsion of these clots from the uterus may cause intense dysmenorrhœa. The treatment consists in increasing the tone of the uterine muscle, and so checking the menorrhagia. This is best accomplished with calcium salts and pituitary extract (infundibulin).

OTHER DISORDERS OF MENSTRUATION.

Mastidynia, or pain in the breasts, occurs, normally to some extent at menstruation; but it may be so severe as to incapacitate the patient. In these circumstances, it will usually be found that the menstrual cycle is prolonged; that is to say, instead of there being a twenty-eight day cycle it

may be extended to thirty-five days.

I have found that the administration of two grains of dried thyroid gland, administered every night from the twenty-first day from the commencement of the previous 'period,' will often cause menstruation to appear earlier, that is at the normal time (twenty-eighth day). If this can be effected, it will be found that pain in the breasts is not experienced to the same extent as previously.

Hystero-epilepsy.—This condition is due to the depletion of lime salts from the tissues, which may occur in an excessive degree at menstruation. The administration of calcium lactate may sometimes entirely cure the condition; but when this treatment is unsuccessful alone, the administration of pituitary extract (infundibulin) as well as calcium lactate will often produce the desired effect of maintaining a high calcium content of the blood and tissues.

DISORDERS OF THE MENOPAUSE.

The menopause is, of course, brought about by the cessation of the ovarian functions and the accompanying changes in the rest of the endocritic system. It is not surprising, therefore, that hormone therapy plays a large part in the treatment of the disorders from which women may suffer at this time of life. The chief symptoms that are amenable to hormone therapy are: (1) circulatory; (2) general metabolic; (3) those arising from outspoken derangements of the endocritic organs; (4) psychical.

Circulatory disturbances.—The "hot flushes" and "cold sweats," from which these patients usually suffer, are due to rapid alterations in the vasomotor control of the superficial vessels. These changes probably occur as the result of the variations in the stimulation of vasomotor nerves by the secretions from the endocrinic organs. Normally, the stimuli are balanced so well that sudden changes do not occur, but the irregularity of the ovarian secretion at the menopause may upset the balance, with the result mentioned.

Now if we can maintain the blood pressure at a high level by contracting the arterioles, then vaso-dilatation does not occur to the same extent. For this purpose, infundibulin in doses of two grains, twice a day, is most useful. It is,

however, inadvisable to continue the administration of this preparation for too long a period, lest the patient suffer with the effects of a continued high blood-pressure, and possibly develop arteriosclerosis. I remember one woman whose blood-pressure was found to be equal to that of 210 mm. Hg., after she had been taking pituitary extract for a month.

In a general way, it is best to begin treatment with this extract, in order thoroughly to control the blood-pressure and keep it at a high level for a week, and subsequently to administer calcium lactate, which has a similar but more moderate effect. Ovarian extract may be given in combination with the pituitary extract or the lactate of lime, in order to mitigate the symptoms which, as already stated, have their origin in the irregularity of the ovarian secretion.

General metabolic disturbances.—At the menopause, women frequently become adipose, and with this adiposity are often associated mental apathy and lassitude. These are signs of alterations in the general metabolism, especially in regard to carbohydrates. This state of affairs is probably brought about in part by pituitary insufficiency ; but the thyroid also may be undergoing atrophic changes. In the treatment, however, of this condition, thyroid gland extract appears to have a better effect than that of the pituitary. Probably the best effect of all is obtained by thyroid and ovarian extracts, given in the manner already described.

Disorders of the endocrinic organs.—During the re-establishment of the balance of the internal secretions, which takes place at the climacteric, some member of the endocrinic system, other than the ovaries, may undergo changes far in excess of the normal or of those which merely give rise to adiposity and other metabolic disturbances of similar importance. The thyroid is the only organ in which such changes are at all frequent or easily recognizable. Exophthalmic goitre is occasionally seen, but is not nearly so common as myxœdema. The former may be treated with infundibulin, and the latter in the ordinary way with dried thyroid gland.

Psychoses.—The mental depression, from which women may suffer at the menopause, is greatly relieved by thyroid administration. This seems to point to the fact, that atrophy of the thyroid with lessened secretion is the principal factor

in producing this psychical phenomenon. It is of great importance that the initial stages of mental depression or melancholia should be relieved, for it is impossible to foretell what course any case will follow, unless the patient has a psychopathic family history, in which circumstances the prognosis is serious. As a rule, these patients have actually ceased to menstruate before mental symptoms arise.

The psychical disturbances that occur during the menstrual irregularity, which often precedes the menopause, are of a different character. The patient is usually irritable and hysterical, and suffers with rapidly changing moods. In these circumstances, there is probably no decrease in the thyroid secretion. If hormone therapy be attempted, pituitary extract will prove of the most value, especially when combined with ovarian extract.

Orchitic extract, also, has been used for disorders of the menopause, but it is impossible at present to speak with any certainty as to its value.

HORMONE THERAPY IN OBSTETRICS.

It may be said at once that, except in the conduct of labour, very little use has been made of hormones in the treatment of the various disorders of conception.

STERILITY.

I find it stated in text-books that obesity is responsible for amenorrhœa, scanty menstruation and sterility. The truth is that obesity occurs as a metabolic disorder resulting from insufficiency of certain of the endocrinic organs, which at the same time produces genital inactivity. Obesity and sterility may, therefore, be phenomena produced by one and the same pathological lesion. For instance, myxœdema leads to obesity and mucoid changes in the subcutaneous tissue, together with amenorrhœa and sterility. As already stated, I have known a patient, in whom this disease was established with the symptoms enumerated above, to menstruate regularly and conceive after treatment with thyroid extract. But, as indicated, it is not only the most pronounced insufficiencies of the thyroid and pituitary which should be treated, but the minor insufficiencies associated with sterility as well, which

are probably more common, although not so easily or so frequently recognized.

DISORDERS OF PREGNANCY.

Abortion.—Since the implantation of the ovum is supposed to depend upon the development of the corpus luteum with its internal secretion, it is possible that habitual abortion may be due to insufficiency in this respect. At the same time, I have shown [7] that the influence of the ovary appears to be greater in this respect in animals than in the human subject.

I have not as yet had sufficient experience to justify an expression of opinion as to whether heterogeneous luteal extract has any beneficial action in preventing habitual early abortion. Great scientific difficulties present themselves in the investigation of this matter. The definite recognition of luteal insufficiency is impossible ; consequently, the administration of the extract cannot be said to *prevent* abortion, should this not occur in any given case so treated. Further, it is highly probable that in this special action luteal secretion is specific to each species. I have, moreover, seen abortion apparently produced by thyroid insufficiency. In stout women with habitual abortion, therefore, thyroid extract should always be given in small doses at night.

Osteomalacia.—In this disease there is abstraction of the lime salts from the osseous system. As a result, great deformity of the pelvis, and of other bones, through which the weight of the body is transmitted, is produced. It appears that during pregnancy there is a great drain on the stored calcium for the benefit of the fœtus, and the disease is greatly aggravated. Formerly, removal of the ovaries was the only known treatment, and this has been held to indicate that there is hyperplasia and over-secretion of these organs, leading to excessive excretion of calcium salts. I have myself shown that removal of the ovaries lessens the excretion of calcium in the urine.[4]

Bossi of Genoa,[8] however, advocated the administration of extract of the suprarenals—that is, of the medulla—and stated that it produces a very beneficial effect on the course of the disease. I suggested that infundibulin might have a similar effect, and this has been found to be the case. Therefore, as might

be expected, those hormones which are antagonistic to the ovarian, in regard to the metabolism of lime salts, are of the greatest assistance in the treatment of this disease.

Psychoses.—The mental disturbances, which occur during pregnancy and in the puerperium, are usually of the melancholic type. In these circumstances, thyroid extract may be given with the greatest benefit, in addition to the careful watching and feeding which are also required.

Eclampsia.—Some years ago, Nicholson published several papers,[10, 11] in which he endeavoured to prove that eclampsia was due to thyroid insufficiency. Experiments performed by me[4] show that this point of view is not correct, at any rate, so far as cats are concerned. Nevertheless, I have myself seen excellent results from the administration of thyroid extract, hypodermically, in the pre-eclamptic state. That the results were entirely due to the thyroid extract I doubt, as other measures—dietetic and so on—were also employed. It is probable, however, that pre-eclampsia and eclampsia are benefited by thyroid extract, in conjunction with other measures; but the treatment cannot be considered specific.

PARTURITION.

What the actual determining factors are that produce labour we do not know, although we may surmise. There is, however, one hormone—infundibulin—which has come to be used with considerable frequency in labour. In 1909, I published the first clinical paper on the subject,[1] after having previously recorded experimental results.[2] Since that date, many hundreds of papers have appeared.

Infundibulin increases the force and frequency of uterine contractions during labour, and also assists retraction during the puerperium. Apparently, it does not interfere with the effects of ergot, but, rather, augments them. Infundibulin should, in the circumstances, be administered intramuscularly.

The indications for its use appear to be many, but a word of warning is necessary. It has been stated that pituitary extract takes the place of forceps. Such a dictum is dangerous. The accoucheur must first be absolutely certain that labour cannot be obstructed: the maternal parts, the child and its attitude must be normal in every respect. Several cases

of rupture of the uterus have already been reported; consequently, great care must be exercised in the use of this preparation before the delivery of the child.

All the other conditions being satisfactory, it may be given with advantage in moderate degrees of uterine inertia occurring during the second stage, although cases of "tetanic contraction" have been said occasionally to follow its administration. The chief obstetrical use, however, of infundibulin is in post-partum hæmorrhage. The effect produced is more powerful and more lasting than that which follows the use of ergot. If the placenta be in the uterus when the hæmorrhage occurs, it must immediately be removed before the uterus contracts tightly down upon it, after the injection of infundibulin. I have, moreover, injected infundibulin into the uterus itself after the child has been delivered by Cæsarean section, with excellent results.

THE PUERPERIUM.

Lactation.—It has been shown by Ott and Scott[12] and others that infundibulin can produce a sudden and profuse flow of milk in the lactating animal. But so far this preparation has proved disappointing clinically. The galactogogue effect is transitory, and it is doubtful if a continued increase in the secretory activity in the breasts is produced. The immediate result of the injection of the infundibular extract is, no doubt, partly due to the expression of the milk contained in the breasts at the time.

Subinvolution during the puerperium, due to constitutional causes, may be treated successfully with infundibulin.

I have not mentioned suprarenal extract in connection with uterine atony and subinvolution, for it is not so powerful or lasting in its effect as infundibulin.

Retention of urine and intestinal atony, subsequent to parturition are best treated by intramuscular injections of infundibulin, in doses of 1 cc. of a 20 per cent. solution. With regard to the retention of urine, it is advisable to let the bladder be full when the injection is first given.

The foregoing, then, is a brief outline of the present position in clinical gynæcological and obstetrical practice

of hormone therapy. It is more one of promise than actual fulfilment, except in a few conditions in which treatment has become established. Scientific treatment follows in the wake of physiological and pathological discoveries, and it is inspiring to know that specific hormone therapy has not yet overtaken our scientific knowledge of these aspects of the subject.

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THE USE OF HORMONES IN CHILDREN'S DISEASES.

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THE rational use of hormones in children's diseases, as in all other conditions, must depend upon our conception, not only of the functions of particular secretory glands, but of the interrelationship of the various internal secretions as well. Thyroid extract, for instance, has now been prescribed for almost everything, and, according to innumerable authors, with good results. In consequence, the number of symptoms attributed to thyroid deficiency continually increases. Yet, when we come to continued clinical trial, which is the crucial test, we find that thyroid treatment will overcome a given symptom in one case and utterly fail in another.

As an example, nocturnal enuresis frequently yields to small doses of thyroid extract. It is often made worse by large doses. It is sometimes uninfluenced either by large or small doses, and I have known it arise for the first time during a course of thyroid treatment for some other condition, and to cease on withdrawal of the remedy. In the face of these facts it is still rational to give thyroid treatment a trial in any case of enuresis, which, by the way, is often diurnal as well as nocturnal, because more often than not such treatment is successful. But it is manifestly no longer rational to say that the cause of nocturnal enuresis is thyroid deficiency. The cause is evidently some other factor which is partly regulated by, or at least correlated with, the activity of the thyroid gland. Such a factor may possibly be found either in the pituitary or suprarenal glands. Polyuria has in certain cases been found associated with lesions of the posterior lobe of the pituitary, and, clinically, the injection of adrenalin usually causes an increase of urinary secretion. Although polyuria is not precisely the same thing as enuresis, there

is sufficient analogy to warrant the above suggestion.

Another example worthy of consideration is furnished by urticaria. This condition is common in childhood, either in the form of acute attacks, to which some children seem specially liable, or as the more obstinate condition termed "urticaria chronica infantum." Both conditions sometimes clear up rapidly under thyroid extract, which is specially valuable for the chronic type. On the other hand, I have several times witnessed the occurrence of urticaria in children under thyroid treatment, and this urticaria has rapidly got well on withdrawal of the medicament. Clearly, then, we must not look on urticaria as a symptom of "thyroid deficiency," though apparently it does depend on some condition rather closely connected with thyroid activity. Such a condition may be of toxic origin, as illustrated by the occurrence of urticaria after eating stale fish, in which case it is unfair to blame the thyroid, except in so far as we believe this organ to have a powerful influence in neutralizing or destroying poisons, and, therefore, the more active the thyroid, the less the risk of toxæmia. Or the urticaria may depend upon poverty of calcium salts in the blood, a supposition supported by the commonly favourable influence of the administration of calcium salts. This type of urticaria is prone to occur after indulgence in acid drinks or fruits, such as lemonade or plums, and is very amenable to treatment. But the balance of calcium salts should not be so low that it can readily be upset by a relatively trivial cause. We believe that calcium metabolism is largely under the influence of the ductless glands, and this aspect of the subject must be considered further. There are plenty of clinical and experimental facts which illustrate the complexity of calcium metabolism, and how hopeless it is to discuss the action of a single internal secretion without considering the influence of the others.

The influence of thyroid in promoting calcium assimilation is best exemplified by cretinism. Everyone is familiar with the fact that an enormous rate of growth may be obtained by the administration of thyroid extract to young cretins. I have personally obtained a growth of eight inches in a year in the case of a boy, not strictly cretinous, aged 14 years, but in

appearance resembling a child of 8. But other more striking figures than this have been published. I have also met with a cretin, whose growth, under thyroid treatment, was reported to have been four inches after he had attained the age of 40 years, and some of his deciduous teeth were then present. It is, however, difficult to see how bony growth can take place when ossification of the epiphyses is complete, and an X-ray examination of these should be made before embarking on a long course of treatment. The presence of the deciduous teeth, in the case just cited, might possibly be taken as an indication of delayed maturity. As a rule, striking results must not be expected in mature life.

Thyroid activity is probably not the only factor upon which growth depends, yet we may fairly state that when thyroid activity is defective, growth is likely to be stunted, and further, that in the case of children thyroid treatment usually promotes growth. And, since the lack of growth in cretins is principally noticed in the limbs, we may reasonably state that the thyroid has a special influence upon the ossification of the long bones, and, presumably, in some way enables the body to make use of the available calcium supplies. But we must also note the opposite fact that in Graves's disease, or under the influence of excessive thyroid feeding, there is an excessive elimination of calcium, both in the urine and in the fæces. It is evident, therefore, that calcium deficiency may result either from thyroid insufficiency or over-activity; accordingly, we may meet with conditions which are partly dependent upon the calcium content of the blood in either state. This enables us to understand why urticaria can sometimes be cured with thyroid treatment, and, on the other hand, is sometimes a direct result of thyroid treatment.

The same argument may be applied to the calcium factor in hæmorrhagic conditions, such as epistaxis, menorrhagia, and perhaps purpura, as well as chilblains, and a tendency to bruise excessively from trifling injuries. Some headaches also seem to depend upon calcium deficiency, and I believe the main factor in dental[16] caries to be the absence of an adequate supply of calcium salts in the saliva. Normal saliva is alkaline, and this alkalinity should be sufficient to neutralize any acid products of fermentation arising

from bacterial decomposition of food particles. The dental profession is quite agreed that the primary stage in dental caries is decalcification of the dentine by acids thus arising. It is difficult to see how this would occur in the presence of an adequate supply of saliva charged with its natural ingredient, calcium bicarbonate. Further, it is to be observed that the lower front teeth, which from their position are constantly bathed in saliva, show a very marked immunity from dental caries, and are in fact usually lost late in life, not from caries, but by getting loose and falling out. Their immunity from caries has been attributed to their shape, which is supposed not to favour the retention of food particles, but in reality their shape does not strikingly differ from that of the corresponding teeth in the upper jaw which are highly susceptible to caries.

The subject cannot further be dealt with here, but has been discussed at length by the writer in the *British Dental Journal* for July 15, 1913.[1] We may note, however, that the submaxillary saliva is richer in calcium salts than the parotid, and in consequence, when a shortage of calcium occurs, the parotid saliva suffers first and becomes acid. Hence the back teeth are the first to decay. In many cases, I have been able to restore the alkalinity of the saliva in children by thyroid treatment. But here, again, excessive thyroid activity should theoretically do harm by promoting excessive excretion of calcium. It is to be remarked that patients with Graves's disease undoubtedly suffer from excessive dental caries. In children, therefore, with an undue amount of caries, the thyroid factor must be considered. Those who are deficient in thyroid are likely to be backward in cutting their teeth, or to suffer from overcrowding of the teeth and irregularity of the dental arches,[16] owing to defective development and inadequate calcification of the jaw, a condition akin to rickets. But excessive caries of the temporary teeth is often found in children who are full of life and energy, though perhaps also nervy, and in these cases the poverty of calcium is, I think, referable to excessive thyroid activity resulting possibly from previous children's complaints, or sometimes from a mild and not always obvious infection with tuberculosis.

Epilepsy and tetany are two other diseases bearing some relationship to calcium metabolism. Thyroid sometimes does good in epilepsy, especially in those cases accompanied by lethargy and general dulness of disposition. It may act here by improving calcium metabolism. In some cases of epilepsy, thyroid seems to do harm rather than good, and possibly these cases would do better on calcium salts, which are often distinctly valuable in epilepsy. Calcium salts have a general sedative influence upon nerve tissues, and are of well known value in tetany. Tetany is now attributed to defective action of the parathyroid glands, but it may be produced by removal of the thyroid only, especially under the superadded influence of pregnancy, which makes extra demands on the calcium supplies. On the other hand, a case of tetany has been published[2] resulting from an accidental overdose of thyroid tablets in a child, so we again have evidence that the thyroid may be indirectly responsible for the same result either by inertia or over-activity.

This naturally increases our difficulties in knowing whether to prescribe thyroid or not in a given case. Chilblains are usually benefited by thyroid treatment, especially if given in conjunction with calcium, but they occur in Graves's disease as well. We must bear in mind, however, in making deductions from clinical observation of Graves's disease, that in cases of long standing there is frequently some degeneration of the thyroid gland, and the whole condition may pass into the diametrically opposite one of myxœdema. This change is not likely to occur suddenly but gradually, and consequently there are likely to be periods of partial, or temporary, thyroid exhaustion, when symptoms may be mixed.

But calcium metabolism is under the influence of other ductless glands beside the thyroid. Experimental removal of the thymus in very young animals has produced a condition resembling rickets.[3] The long bones have become soft and crooked, and experimental fractures have been slow to unite. The thymus normally appears to atrophy at puberty.[4] Its atrophy can be hastened by breeding from young animals, and conversely this atrophy is delayed by castration. The effect of castration, and therefore possibly of

persistence of the thymus, is to delay ossification of the epiphyses, and produce increased length of the long bones. Long arms and legs are said to be an indication of late maturity, and animals which mature early are usually short in the leg.[5] Shortness of the legs has been produced experimentally by feeding young hens on ovarian substance.

Women mature earlier than men, and on the average, of course, are of less stature. Also the natives of hot countries, who mature early, are usually of short stature. The thymus is particularly rich in phosphorus and may be more intimately connected with phosphorus metabolism rather than that of calcium. But since calcium exists in the body largely as calcium phosphate, any such influence is bound to affect calcium as well. I have not used thymus at all extensively in children's diseases, but it certainly should be worth trying in rickets, deficient stature, and possibly in cases in which it may appear desirable to postpone the arrival of puberty. Theoretically, it might be valuable too in cases of eroticism, masturbation, or precocious sexuality. I have given it, with benefit as I think, in a case of spermatorrhœa. The patient, aged 21, gained a stone in weight and improved greatly in physique in a few months' time, but there were other factors which may have been responsible for these effects. Adrenalin was subsequently found to control the spermatorrhœa more adequately. The influence of the pituitary gland upon calcium metabolism is evidenced by the changes resulting in acromegaly, in which we have increased growth in certain bones.

The ovaries, on the other hand, are responsible apparently for increased calcium excretion, the menstrual fluid being richer in calcium than ordinary blood. Ovariotomy has sometimes proved to be a successful measure in osteomalacia. Lastly, the suprarenal glands have an important influence on calcium metabolism. It was found by Blair Bell[6] that, after removal of one suprarenal gland in the case of two rabbits, calcium excretion was enormously increased, and in one of the animals the legs became bent. Further, in cases of human suprarenal tumour, in which there is evidence of over-activity of these glands, precocious skeletal growth accompanied by early sexual development is the rule. A case has been recorded[7] of a girl of 7 who was as tall as a person of 20.

Growth, of course, is general, but it implies remarkable calcium anabolism, greatly contrasting with the stunted growth of cretinism. If, therefore, thyroid activity is essential to growth, we may equally argue that suprarenal activity is an enormous stimulus.

Good results have already been recorded in stunted growth by the use of thyroid, thymus, and pituitary extracts. Possibly we shall yet obtain greater results with suprarenal preparations. I have only made notes of one case with any bearing on the subject, and that is inconclusive, because the patient was not short to begin with, being 5 feet ½ inch in height, and she was 12½ years old, an age when girls often do grow enormously both in height and weight. The case, however, is perhaps worth recording for other reasons. She was brought to me on account of constant fatigue, "bilious" attacks, and fainting. She was very nervous as well. Examination of the urine revealed the presence of a good deal of albumen in the afternoon and evening, but the morning sample was nearly free. She was first given calcium salts and thymus, and, after a few weeks, tablets of desiccated suprarenal gland, gr. ii. t.d.s. (P. D. & Co.). The result was excellent. Nervousness and fatigue disappeared, urine became free from albumen, and in 6 months there was a growth of 1¾ in. in height, and 11½ lb. in weight, but menstruation did not appear.

Although the growth may have been incidental, there is no reason why the improvement in health should not be accredited to the remedies employed, which were all given with a definite object in view, namely, the thymus, to postpone menstruation, which might have contributed further to the existing debility; the calcium, for its influence upon "functional" albuminuria, which may depend upon deficient coagulability of the blood, and the suprarenal gland both for its possible influence in promoting the absorption of the calcium and for its effect upon the blood-pressure, which would naturally counteract the tendency to faint. Adrenalin raises the blood-pressure in a twofold manner—first, by constriction of the arterioles, and, secondly, by a definite stimulating influence upon the heart. It removes fatigue products from the muscles as well, for it has been shown that a

frog's muscle when worn out by stimulation can be resuscitated materially with adrenalin. It probably assisted, therefore, in the case just cited, in removing the sensation of chronic fatigue.

With regard to the use of thyroid and suprarenal preparations in children, we are of opinion that the two glands work in very close harmony, and that many of the effects obtained by thyroid medication are produced because the thyroid stimulates the suprarenals. There is plenty of evidence to support this statement. It has been found that 10 grains of thyroid gland, administered thrice daily to rats, cause death in about 20 days from congestion and hæmorrhage into the adrenals. The dose is enormous in relation to the size of the animal, but it shows that thyroid, according to dosage, may produce simple hyperæmia and increased activity or extreme congestion and destruction of the suprarenals, with corresponding results.

In Graves's disease, according to Biedl,[5] the amount of adrenalin present in the blood has been found to be from four to eight times the normal quantity. It is not improbable that many symptoms of Graves's disease, which may all be imitated by excessive thyroid feeding, are in reality due to the resulting activity of the suprarenal glands. The immediate effect of an injection of adrenalin is a violent and rapid heart action, and a general tremor, symptoms most strikingly characteristic of Graves's disease. Further, these symptoms come on so rapidly after the injection of adrenalin, and disappear so soon, that it is difficult to suppose they are due to any stimulating effect, which the adrenalin might conceivably have upon the thyroid gland. There is also a decidedly increased elimination of urine. The same symptoms can be produced by large or continuous doses of thyroid, but they take much longer to develop and to disappear, which would naturally be the case if they result from a secondary suprarenal activity.

The somewhat dilated pupil, frequently present in Graves's disease, is probably an adrenalin mydriasis; whilst exophthalmos, except in so far as it depends upon an actual deposit of fat in the back of the orbit,[8] which after all may be a secondary result, is usually attributed to irritation of the sympathetic nerve,

another result of adrenalin. I treated one of my cases of Graves's disease for a month with adrenalin chloride. Her goitre certainly diminished considerably, and she slept much better, having previously been long troubled with insomnia. Her tremor, however, became so much worse, that she was often quite unable to do simple things like fastening a button. This excessive tremor disappeared in a few days on leaving off adrenalin, and resuming her former mixture of Tr. Iodi ɱv. t.d.s c. aq. Seeing that the blood of Graves's disease cases already contains an excess of adrenalin,[8] there is little ground for hope that suprarenal treatment of these cases will be uniformly successful, although such treatment was highly lauded by the late Dr. Gibson of Edinburgh. Many subsequent observers have already recorded want of success in the attempt to follow in his footsteps.

Insomnia is a very characteristic symptom of thyroid influence. Thyroid treatment, if carried to even slight excess, has a very stimulating effect. I have seen insane persons, who were previously docile, become very intractable and excited under the influence of the medicine, and I have found, too, that children get very excitable under its influence. A child of six once said to me, "Do give us some more of that medicine we had last time, it makes us so excited, and I do like being excited." His mother confirmed the observation in the case of this boy, and her other two children, on several occasions when they were taking thyroid, although she did not know what the remedy was. This must be taken as an indication for withdrawal of the remedy.

It is a very tempting supposition that many, or even most cases of excitable or highly nervous and energetic dispositions are associated with ample or excessive thyroid activity. We find the same type of disposition in women at the menopause, which is probably referable to undue thyroid activity.[9] The point is mentioned because, in such a case under my care, suprarenal tablets proved to be a remarkable sedative and a remedy for insomnia of long standing. Childhood is essentially the age of excitability, restlessness, and a highly strung nervous system, and the writer believes that these characteristics depend upon thyroid

activity in much the same way that boldness and courage are associated with sexual vigour. The difference between a castrated and entire male in domestic animals is well known. The stag, a most timid creature at other times, often becomes highly dangerous in the rutting season. The same law is said to hold good in the case of eunuchs,[10] and need we contrast the shyness of the "maiden of bashful fifteen" with the boldness of the wanton?

Our opinion, then, is that in children the thyroid is more often (relatively) over-active than not; that children bear thyroid activity well is evidenced by the fact, that they very seldom get Graves's disease. The ample secretion is probably used up in the processes of growth and development. On the other hand, the suprarenal glands of children are found to have suffered severely[11] in fatal cases of such diseases as measles, diphtheria, pneumonia, etc. It is probable that the brunt of all infections and intoxications falls upon both thyroid and suprarenals, the latter probably being the more important of the two. If, as we think, thyroid activity is the natural precursor of suprarenal activity, it follows that when the suprarenals are, for the time being, incapable of adequate response, we should get a period of continuous hyper-activity of the thyroid; this would in turn be lessened, when an adequate supply of adrenalin was forthcoming, by reflex constriction of the blood supply to the thyroid gland, an effect[11] which is among the physiological results of an injection of adrenalin. Hence, we should expect a condition of increased thyroid activity, which in turn may lead to exhaustion, as the result of any illness or infection of childhood.

The symptoms of such increased thyroid activity are very common in childhood, in the form of undue excitability, nervousness, sleeplessness, rapid growth accompanied by thinness and inability to put on weight, and dental caries, owing to excessive calcium elimination and consequent defective alkalinity of the saliva. If the process be carried on further, we may get a period of thyroid exhaustion, with certain resulting symptoms of myxœdema; but this condition is very much less common than the other. Curiously, in either condition thyroid treatment will often do good, but up to a certain point only. In the first class of case, the

artificial supply of thyroid acts as an additional stimulus to the suprarenal glands, and temporarily evokes an adequate response; in the second case, it would assist the partially exhausted resources of the patient's own thyroid.

In either event, if nature ordains that a certain pathological condition of the body shall be met by increased thyroid activity, it is perfectly rational to help her by giving more, so long as we do not, so to speak, make the mistake of drowning a child that was merely asking for a drink. When, therefore, we administer thyroid to children, the remedy should be left off, tentatively, as soon as the expected result has been attained. It can easily be given again if necessary, but except in cases of deficient growth, dulness of intellect, or general lethargy suggestive of myxœdema, I have usually found that thyroid treatment rapidly improves the patient up to a certain point and no further. This is easily understood, if our theory, that it acts by stimulating the suprarenal glands, is correct.

It is hardly good policy to over-stimulate a tired organ. As an illustration of this point, I may cite a case which improved on thyroid, but rapidly recovered when given suprarenal tablets. The patient was a boy of about 14, whose unconquerable habit was to touch things with the knuckles of his left hand. If, attempting to overcome this trick, he succeeded in resisting the impulse to touch a given object, he soon became so restless and perturbed that he had to go back and touch it, in order to obtain peace of mind. Of the pathology of such cases, I know nothing. He had already received innumerable "tonics," and, obviously, the only line of medicinal treatment was to attempt to improve his general health. Accordingly, a trial was made for several weeks with thyroid extract. His father was quite definite that this medicine was doing more good than anything the boy had taken previously. But as inspection showed that the knuckles of the left hand were still very dirty, and, therefore, that the habit was still very bad, it was decided to try suprarenal tablets instead of thyroid. The boy now rapidly improved, and six weeks afterwards was reported to be quite well.

I have seen considerable improvement in athetosis, in an imbecile child, under thyroid treatment. The mental con-

dition also improved a good deal. Chorea is another complaint which sometimes improves under thyroid treatment. I have not as yet tried suprarenal extract in either of these conditions. Suprarenal extract is not very easy to give as a remedy, because it oxidizes so readily that there is always an element of doubt as to how much has really been administered. Hypodermic injections of adrenalin are frequently painful afterwards, and are obviously unsuitable for repeated administration. It is said that if the remedy be held under the tongue for a few minutes before swallowing, absorption takes place from the mucous membrane. I have obtained undoubted results by this method, as well as by the administration of tablets, though it is quite possible that the quantity absorbed is much less than that administered. In cases of grave emergency, it should be given, in a pint[1] of warm, normal saline solution, subcutaneously. The apparatus for this purpose can readily be extemporized with the needle of an anti-toxin syringe, and some glass- and rubber-tubing, like that sold for the old-fashioned feeding-bottles. The needle is introduced under the skin of the anterior fold of the axilla, after having been connected by means of the tubing to a jug of normal saline at 105° F., or warmer if thought advisable. It is preferable to have a needle in each axilla, either duplicating the apparatus, or by using an inverted T shaped tube, if one be at hand. The vertical limb of the T, in this case, is connected with the rubber-tube going to the jug, and the two ends of the horizontal limb are connected with the needles. The easiest way to keep the end of the tube in the jug is to use an inverted U-shaped tube, one limb of which is inside, and the other outside, the jug. With a very little ingenuity all this can be done single-handed in any country cottage, and it is therefore preferable to the business of inserting a cannula into a vein. It is possible that some young lives might be saved by these measures, especially in cases of toxæmia from illnesses which are usually short and acute, like diphtheria, measles, and pneumonia. The saline, of course, dilutes the toxins,

[1] Three ounces of saline solution is as much as can conveniently be infused into one axilla of a child a year old. The quantity may, of course, be increased according to the age of the child, or to replace fluid previously lost from the body by diarrhœa, hæmorrhage and so forth.

aids in their excretion by skin and kidneys, and the adrenalin is a potent detoxicating agent, as well as the most powerful stimulant we possess. From 10 to 20 drops of a 1 in 1,000 solution of adrenalin may be added to the saline solution. It might be well to use half the quantity to begin with, as more can easily be added if needful, but given in this way the drug is absorbed so slowly that there is little fear of an overdose. Small doses of adrenalin given by the mouth are sometimes most useful in whooping-cough. A child of two will take 2½ or 3 minims, six times in 24 hours, without any obvious result, except that vomiting and frequency of whooping attacks are greatly lessened. Both the duration and the severity of the complaint seem to be greatly improved by this treatment. It has been shown, experimentally, that an injection of adrenalin has a special effect upon the mucous membrane of the nose,[11] causing vaso-constriction, and this action probably accounts to some extent for its value in asthma and hay-fever, both of which complaints are often dependent upon some form of nasal hyperæmia.[12] An hypodermic injection of adrenalin will often cut short a paroxysm of asthma in a marvellous way, but it does not necessarily cure the complaint, and repeated injections would probably have a very deleterious action upon the sufferer.

This selective action of adrenalin upon the nasal mucous membrane, which is shared by pituitrin,[5] suggests that enlarged tonsils and adenoids, which so often accompany an engorged and hyperæmic nasal mucosa, may in reality depend upon temporary suprarenal exhaustion. The status lymphaticus has been attributed by certain authorities (Wiesel and Hudinger[8]) to hypoplasia of the chromaffine system. The status lymphaticus, in all probability, is merely an extreme form of the condition which is present in a mild degree in all cases of enlarged tonsils and adenoids. At any rate, the two conditions are commonly indistinguishable, until we meet with an "anæsthetic death" in some case about to undergo operation, when the post-mortem examination reveals the presence of an enlarged thymus and enlargement of internal lymphatic glands; we may, therefore, not unreasonably regard the two conditions as one of degree.

Enlargement of tonsils and growth of adenoids are particularly prone to occur in children as a sequela of any

debilitating illness, perhaps especially measles, in the fatal cases of which serious[11] lesions of the suprarenal glands may commonly be demonstrated. It is a reasonable argument, therefore, that ordinary cases of "tonsils and adenoids" *may* depend upon temporary suprarenal exhaustion. As to treatment, I have not yet had an opportunity of coming to any conclusion upon the value of suprarenal treatment of such cases; in addition to this, we have to contend with the factor that suprarenal opotherapy is as yet a very inadequate remedy for suprarenal deficiency. I have, however, frequently obtained good results with thyroid, for which suggestion I am indebted to Leonard Williams.[13]

My experience of these cases is that they invariably improve temporarily, and many of the slighter cases may thus be saved from operation. But, on the other hand, when thyroid treatment is left off, nasal obstruction often tends to recur, especially after a cold or a visit to the swimming-bath, which, in these cases, is also rather frequently responsible for deafness. In such cases, the advisability of operation must be considered, although it is really remarkable how quickly snoring can be stopped and nasal breathing acquired under the influence of thyroid. But if, in accordance with our view, the thyroid acts here by stimulating the suprarenals to greater exertion, we cannot expect this to cure the condition, because a period of further exhaustion must frequently be the natural result of such stimulation. Curiously, enlargement of the tonsils and some degree of hypertrophic rhinitis are commonly present in Graves's disease, and Leonard Williams remarks on the frequent occurrence of nasal catarrh as a result of prolonged thyroid medication.[13] These contingencies are easily explained, in accordance with our view, as being the result of suprarenal fatigue produced by over-stimulation.

Further, it may be remarked that Addison's disease has been recorded, in rare instances, as a complication of Graves's disease, and that, in the latter, pigmentation to a slight degree is extremely common. The presence of lymphatic enlargements, in association with abnormalities of thyroid and suprarenal activity, is almost certainly a process of defence. The thyroid, no less than the suprarenals, is concerned with the production of immunity. The lymph glands are the

source of the white blood corpuscles, or lymphocytes. The thyroid, according to Falta, stimulates the formation of erythrocytes and mononuclear leucocytes, and thyroid insufficiency diminishes the number of the red blood cells. It is in accordance with my own observations that adequate thyroid activity is usually accompanied by a good colour, and thyroid is a most valuable adjunct to iron in the treatment of anæmia. Sajous believes the thyroid secretion to be synonymous with Wright's opsonins.

We cannot here discuss questions of immunity, but if the foregoing conclusions are correct, it is obvious that we may meet with various degrees of over-activity or exhaustion in one or other of these essential organs as the result of any general systemic infection. We may state broadly, that after any illness in childhood, thyroid extract judiciously administered acts as an excellent tonic. It improves appetite wonderfully, and is an almost unfailing remedy for children that will not take their food. It would probably have saved the chubby Augustus who refused to take his soup, and, in consequence, came to an untimely end. It often corrects constipation, and, more strangely still, checks diarrhœa, especially the variety known as lienteric.

I recently came across an under-sized child of this type, whose bowels, I was told, acted three or four times every day, and had done so "since birth." I ordered thyroid tabloid gr. ½ twice daily. This was on a Saturday night, when he took one tabloid. On Sunday, he had two tabloids, and the bowels acted four times, as usual. On Monday, they only acted once, and have done so ever since. Treatment has been maintained, and the child, naturally, is very much better and gaining weight. There are many other conditions in which thyroid has proved useful in children's diseases, but it is impossible to enumerate them all. It is worth trying, but will not necessarily succeed, in nearly all chronic skin affections. Affections of the cornea, no less than of the skin, will often do well on thyroid. Interstitial keratitis may specially be mentioned; we have seen very rapid improvement in a case of this complaint, which happened to be dependent on tuberculosis and not on syphilis.

With the subject of tuberculosis we must close. Many children suffer from various minor ailments, or are commonly

called "delicate," but the cause of this slight chronic ill-health is not very obvious. They have had their tonsils and adenoids removed, but this operation by no means always produces the marvellous results usually predicted. They may be nervous, or suffer from night terrors, or frequent "bilious" attacks, in which case the existence of the appendix is imperilled. Appetite is capricious, or, although they eat well, they are always thin. Asthma is another burden which may have to be borne. Tubercle is probably not mentioned, but the mother usually gives them cod liver oil, virol, or the latest patent medicinal food, surreptitiously, whilst the doctor is careful to order fresh air. In point of fact, the evidence of tuberculosis is in most cases not sufficient to justify the diagnosis. To such cases I have often given thyroid in small doses, sometimes with considerable temporary benefit, but many cases relapse and are as bad as ever in six months or a year.

Latterly, I have treated these cases with tuberculin, given by the intensive method, with most striking success. Although in each case it would have been very difficult to substantiate the diagnosis, the wonderfully rapid improvement clearly shows that what was the real cause of the trouble. For the technique to be employed in such cases, reference may be made to the tuberculin[15] number of the *Prescriber*, published in November 1913. In the majority of cases, no difficulty arose in treatment. But one or two were very sensitive to tuberculin, and in these cases the interesting point was that a "reaction" produced vomiting, and sometimes diarrhœa, with abdominal pains and tenderness, as well as pyrexia. If tuberculin artificially introduced can give rise to such symptoms, it is exceedingly probable that sometimes when they occur spontaneously they are due to excessive auto-inoculation from some obscure focus.

The almost universal reaction to tuberculin tests obtainable in adults, coupled with post-mortem evidence, amply proves that, practically, we all become infected with tuberculosis, against which the more fortunate, and luckily too the majority of us, in due course acquire adequate immunity. This early infection with tuberculosis occurs commonly in childhood, and is probably one of the most common causes of slight chronic

ill-health. The acquisition of immunity is only produced by frequent auto-inoculations, a process involving considerable disturbance of the immunizing apparatus, amongst which must be reckoned, as we have seen, the thyroid, thymus, and lymphatic glands, the hæmopoietic system generally, and the suprarenals. It is obvious that, amongst these many disturbances, conditions must often arise which may be benefited by such a process as thyroid medication; having obtained a successful result, we are naturally inclined to attribute the cause to thyroid deficiency, and perhaps lose sight of the factor that disturbed the equilibrium of the internal secretions. In short, we focus our attention on Nature's efforts at repair instead of on the primary disease, which, it must be admitted, is often obscure.

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HORMONES IN RELATION TO DISEASES OF THE SKIN.

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Ever since 1893, when Dr. Byrom Bramwell first employed thyroid feeding in psoriasis and certain other scaly conditions, organo-therapy has attracted more or less attention in relation to cutaneous diseases. So favourable were the earlier results from it, that this treatment soon achieved a fame which was subsequently discovered to be out of all proportion to its real merit; its further use led to frequent disappointments, and, like the proverbial rocket stick, it came down from being regarded as a panacea for all manner of scaly dermatoses to being almost entirely neglected.

Recently, however, owing to the researches on the physiology of the internal secretions and the better understanding of their influence and importance, a new interest has been aroused in organo-therapy in skin diseases, not only in connection with the thyroid, but also with other members of the chain of ductless glands, namely, the thymus, suprarenal, pituitary, and genital glands. In this contribution, I will review briefly the present state of our knowledge with regard to the relation of these different glands to the skin in health and disease.

THYROID GLAND.

It was the changes which occur in the skin in myxœdema, and the dramatic manner in which they sometimes clear up under the influence of thyroid feeding, which suggested the employment of this remedy in the treatment of certain cutaneous disorders in which the skin was somewhat similarly affected. In myxœdema, the skin presents a semi-translucent, yellowish appearance, is swollen, inelastic, dry, rough, and

sometimes scaly, is cold to the touch, and does not readily flush but in rare instances may present reddish patches over the malar prominences, and occasionally there may be more or less marked pruritus.

The hair of the scalp may become scanty or more rarely prematurely grey, and there is not infrequently a falling of the hair from the eyebrows, eyelashes, axillæ, and pubes. The nails also may be affected and show signs of dystrophy. There is a diminution of the internal secretion of the thyroid, due to an atrophy or fibrous degeneration of the gland; but when thyroid feeding is instituted and the deficit made good, a marked improvement in the condition of the skin usually supervenes, in which it loses its harshness, exfoliates, becomes smooth and sometimes actually moist, the pruritus disappears, the hair grows, and the condition of the nails may show definite improvement.

Changes in the skin also occur in exophthalmic goitre, in which there is an over-functioning of the thyroid from the disease, and in hyper-thyroidism produced artificially by an excessive dosage of thyroid. In hyper-thyroidism, the skin, instead of being dry, harsh, and scaly, is moist and thin, shows a definite tendency to flushing, and generally presents finely injected patches over the nose and prominent parts of the cheeks. Occasionally associated with the above symptoms there may be pruritus, pigmentary changes, loss of the hair and dystrophy of the nails.

The cutaneous changes met with in hyper- and hypo-thyroidism have been taken as indications for the employment of thyroid treatment in certain affections of the skin, and a considerable number of cutaneous diseases have thus been treated with varying success, such as psoriasis, ichthyosis, xerodermia, chronic eczema, pruritus of undetermined origin, persistent urticaria, lupus vulgaris, alopecia areata, pityriasis, rubra pilaris, lichen planus, and seborrhœic dermatitis.

Sufficient attention does not seem to have been paid in the past to the selection of cases suitable for thyroid medication, and many of the doubtful or negative results which have been obtained were probably due to the remedy having been employed in cases which were wholly unsuitable for its use. Since the cases for this treatment have been more carefully

selected, distinctly better results have been obtained.

It will be advisable to refer briefly to the cutaneous affections in which thyroid medication has been more or less successfully employed.

PSORIASIS.

Up to the present time, psoriasis is the disease which has responded most favourably to thyroid treatment, and a considerable number of cases are now on record in which an attack of psoriasis has been cleared up completely under the influence of thyroid apart from local treatment, or in which thyroid has been found to be a valuable adjunct to local remedies. I do not know of any case, however, in which the disease can be said to have been cured completely by thyroid, and recurrences seem as liable to take place after it as after any other form of treatment. On the other hand, a considerable number of cases of psoriasis have been reported, and there are doubtless many more which have not been recorded, in which the treatment has not been of the slightest benefit; it would appear, then, that thyroid has no specific action on psoriasis, but that there must be some individual peculiarity which causes the disease in certain cases to respond to the remedy.

The precise conditions which render a case suitable for this treatment are of great interest and importance, but, so far, they are imperfectly understood. According to Sir Malcolm Morris, it is only indicated in cases in which the skin affection is superadded to some general condition or disturbance of health on which the thyroid medication exerts a beneficial influence, and he advocates its employment chiefly when the skin disease is associated with adiposity, chronic rheumatism, rickets, or hæmophilia.

It has been found, as a general experience, that it is unsuitable in an acute outbreak of psoriasis, that it does not abort the attack, but may even aggravate it at first, that it should not be given until the eruption is fully out, and that the cases most benefited from its use are chronic cases of long standing. It should be avoided when there is irregularity of the heart, or kidney disease. In certain cases, improvement takes place even under comparatively small doses of the remedy, while in others no benefit appears to be derived till it has been pushed

almost to the limit of toleration, or even till more or less marked symptoms of thyroidism have been produced. As far as I am aware, there are no definite observations on record with regard to the actual state of the thyroid in psoriatics, or of the percentage of cases of psoriasis in which there are signs of hypo- or hyper-thyroidism.

XERODERMIA AND ICHTHYOSIS.

A scaly developmental anomaly such as ichthyosis suggests itself as a suitable cutaneous disorder for thyroid medication, and the remedy has been employed in this connection with favourable results in a considerable number of recorded cases. The precise condition of the thyroid in ichthyosis has not been worked out definitely, and would appear from reports to be inconstant ; but clinical examination of the thyroid, especially in young children, is almost invariably unsatisfactory, as the gland is difficult or impossible to detect by palpation. Winfield described a case of ichthyosis in a child who lived two and a half weeks, at the autopsy of which the thyroid body was found to be absent. Colcott Fox reported a case of ichthyosis in a child of 16 months of age, which improved under the ingestion of thyroid extract, and in whom he was unable to detect any thyroid gland. On the other hand, Paul Rion has recorded a case of fœtal ichthyosis in which, at the autopsy, the thyroid gland was apparently healthy.

Up to the present it has not been definitely proved that the thyroid functioning is constantly defective in ichthyosis.

It must be remembered too, in connection with the thyroid, that an enlarged gland does not necessarily mean an increased secretion from the gland, for the enlargement may be due not to new glandular tissue but to fibrous tissue, and may be associated with an actual diminution of thyroid secretion.

A number of observers, however, have found that definite benefit followed the ingestion of thyroid in certain cases of xerodermia and mild ichthyosis in children, and that when thyroid treatment is started a desquamation takes place, which is rapidly followed by an improvement, the skin becoming smoother and assuming a more healthy appearance. Unfortunately, the improvement usually ceases when the thyroid treatment is discontinued, and a relapse is liable to take place.

and I am not aware of any permanent cure having been effected by it. Still the treatment is of value in cases of chronic eczema on a basis of xerodermia; these cases are not uncommon and are singularly resistant to treatment, but when thyroid is prescribed a general improvement takes place in the state of the skin, so that it reacts more favourably to local remedies.

In two cases of Ichthyosis follicularis with baldness of the scalp and eyebrows in two boys, aged respectively 10 and 13 years, which were under my observation at Charing Cross Hospital, thyroid extract 1½ grains was given daily for 200 days with absolutely no benefit. It is doubtful if these cases belonged to the same category as ordinary ichthyosis, although they appeared to be of congenital origin.

In this connection, reference may also be made to Darier's disease (Psorospermosis follicularis vegetans), which is a peculiar dystrophy of the skin affecting chiefly the pilosebaceous follicles, and may occur in several members of a family. Darier himself suggested that this affection was possibly due to a functional insufficiency of the thyroid, but benefit has not so far followed the employment of the remedy in it.

ECZEMA.

Thyroid treatment has been tried in a certain number of cases of chronic eczema, and in a few of them definite benefit or a complete cure has been claimed from the use of the remedy. The majority of successful cases have been those in which there was some evidence suggestive of defective thyroid functioning, such as obesity or rheumatoid arthritis. Good results from its use have been recorded as well in one or two instances in infantile eczema in fat babies. The only cases of eczema, in which I have seen distinct improvement following the ingestion of thyroid, have been when the condition was superimposed on a basis of mild ichthyosis.

SCLERODERMIA.

From time to time, cases have been recorded in which sclerodermia appeared to have been benefited by thyroid treatment. Its use in this affection was suggested by the superficial resemblance of sclerodermia to the inelastic, swollen skin in

myxœdema. The general experience with regard to the employment of thyroid in this connection, however, has been unfavourable. Bramwell, in a recent communication on diffuse sclerodermia, found that the thyroid was atrophied in one of his cases, but that in two cases in which thyroid was prescribed no benefit was derived, nor did there seem to be any evidence that sclerodermia was a nutritional disturbance in any way comparable to myxœdema.

KELOIDS.

Thyroid ingestion has also been tried in the treatment of keloids, and improvement has been reported from it, both in the amelioration of itching and in the actual softening and involution of the lesion; but such good results have been exceptional.

JUVENILE WARTS.

Cases are on record in which multiple warts in children have cleared up under the influence of thyroid medication. The subject of these warts is particularly interesting. They always have a tendency to disappear at puberty, at which time something happens to the skin rendering it an unsuitable soil for the growth of certain vegetable organisms, such as the microsporon fungus of ringworm and the still unknown virus which is responsible for these infective warts, and it is not inconceivable that the thymus secretion may be a factor which renders the skin susceptible and possibly the prescribing of thyroid may neutralize its influence. They occasionally disappear mysteriously when alkalies, such as lime water or magnesia, are prescribed, consequently it is not to be wondered at that the far more profound influence of thyroid ingestion sometimes causes their involution, but the remedy is by no means constant in its action, and many cases are not influenced by it.

TUBERCULOSIS CUTIS.

A number of writers, such as Bramwell, Radcliffe-Crocker, Pearce Gould, Pringle, and others, have reported favourably of the use of thyroid extract in tuberculosis of the skin and chiefly in Lupus vulgaris. Bramwell has recorded two cases of Lupus, in which a remarkable improvement occurred from thyroid extract, and he regarded the treatment as more effective

than any other form of internal medication, although a complete cure was not obtained. It has been found that ulcerated cases especially respond favourably to the remedy, the ulcers tending to heal under its influence, and that the most suitable cases for its use are those that are acute and actively spreading, while little benefit may be expected in cases which are in the quiescent stage. On the other hand, certain observers state that thyroid may be harmful in tuberculous patients, and may even aggravate tuberculous lesions.

My own experience in this connection has been disappointing, and I have not seen sufficient benefit from the use of thyroid in tuberculosis cutis to warrant its employment, except in cases in which there is some evidence of thyroid insufficiency.

Thyroid treatment has been employed as well in an experimental fashion in a number of other skin diseases, and isolated cases are on record in which benefit has been derived from its use in acne vulgaris, rosacea, leukodermia, seborrhœic dermatitis, rhinophyma, and acanthosis nigricans; but as the failures are rarely mentioned, too much reliance must not be placed on the few isolated successes. Where benefit has been derived in the above affections, it has been most probably owing to their occurrence in an individual in whom the thyroid function was defective.

INFLUENCE OF THE THYROID GLAND ON THE EPIDERMAL APPENDAGES.

Hair.—One of the most characteristic symptoms of myxœdema is a defluvium of the hair, which is liable to become scanty on the scalp, axillæ, pubes, eyebrows, and eyelashes. Another less frequent affection of the hair in the same disease is premature greyness. In such cases, the administration of thyroid results in an improvement in the hair's growth and possibly in a restoration of the pigment. Cases are on record in which alopecia has been benefited by thyroid feeding, and a growth of hair has taken place. Eddowes recorded a case of generalized alopecia associated with leukodermia in a young man in whom the thyroid was absent, and in whom improvement occurred after thyroid extract was prescribed. It has been tried from time to time in Alopecia areata but with doubtful success though probably it would be distinctly beneficial were the Alopecia areata associated with defective

thyroid function.

Nails.—Dystrophy of the nails, in which they become opaque, ridged, irregular, frayed at the edges, and brittle, has been reported in connection with thyroid disease, both in myxœdema and Graves's disease. There is nothing characteristic, however, in the appearance of the nails to suggest that the cause is defective functioning of the thyroid or an increase of its internal secretion, and the changes which occur are similar to those met with in connection with any general disorder which interferes with the nutrition and growth at the nail matrix. Where the dystrophy occurs in association with myxœdema, improvement under thyroid treatment may reasonably be expected.

DOSAGE OF THYROID.

In the treatment of cutaneous diseases, thyroid is generally prescribed in the form of the extract. It is well to begin with small doses so as to accustom the system to the remedy before pushing it, and to be able to detect any idiosyncrasy towards it. As a rule, just as good results may be obtained by comparatively small doses over a prolonged period as by pushing it to the limit of toleration. In certain cases, however, no benefit seems to follow small doses, and it is only when comparatively large quantities have been prescribed and the patient is becoming obviously under its influence and shows signs of tachycardia, tremors, thirst, vomiting, diarrhœa, or other symptoms of thyroidism, that the skin lesions tend to improve.

Infants and young children tolerate the remedy well. In infants, the dose should be one half increased to one grain per diem ; young children of between four and fourteen years may begin with one grain a day, increasing to two and a half; and for adults the dose ranges from two and a half to ten grains per diem. During the time that the patient is under thyroid treatment, he should be watched carefully and the remedy must be stopped if any marked signs of thyroidism supervene.

SUPRARENAL BODY.

The chief influence of the suprarenals on the skin, as known at present, is in connection with pigmentation. In

Addison's disease, in which the suprarenal secretion is defective, there is a marked increase of pigmentation, occurring chiefly in situations normally pigmented, such as the face, neck, arms, hands, nipples, axillæ, anus, and genitalia, which spreads later to unpigmented parts, such as the abdomen and legs, and finally affecting the mucous membranes of the cheeks, lips, gums, and conjunctivæ.

Although various theories have been advanced to explain the connection between the diseased suprarenals and the increased pigmentation, no satisfactory explanation has yet been forthcoming. Suprarenal experiments have been carried out in animals, with the object of trying to produce pigment in them by interfering with the suprarenal function, but these have, so far, given negative results. It is generally recognized that the pigment in Addison's disease consists of melanin situated in the deeper cells of the epidermis. It has been suggested that the melanin is autochthonously produced by the epidermal cells, and that the suprarenal secretion in some way controls its formation, by an increase in the output of the pigment-producing cells when the action of the suprarenal secretion is removed. Another view has been advanced by Halle and Fränkel, and supported by Adami, to the effect that tyrosin is the matrix of adrenalin, and that when the suprarenals are diseased tyrosin is unable to form adrenalin, but accumulates in the skin and elsewhere, being converted by the action of oxydases into a black pigment.

The suprarenals would appear also to exert an influence on the growth of the hair, for in one or two instances hypertrophy of these glands has been associated with early sexual development and growth of hair in the axillæ and pubes. An example of this is recorded by Bulloch and Sequeira in a young girl who became sexually mature at eleven years old and who died from a malignant hypernephroma. On the other hand, disappearance of the pubic hair and non-development of the genital organs have occurred in connection with defective suprarenals.

The only cutaneous disease, in which suprarenal medication has, so far as I am aware, been employed with reported benefit, is rosacea. Good results have been obtained from the employment of adrenalin, in the form of adrenalin chloride 1 in 1,000, in five minim doses, three times daily

half-an-hour before food, and persisted in for several months. (Rothmann).

PITUITARY GLAND.

The relation of the pituitary gland to the skin is not yet understood, though its function has been found to be linked up closely with that of the thyroid, and it has been observed that hypertrophy of the pituitary follows suppression of the thyroid. It has been observed that in acromegaly, in which there is hyper-pituitarism, there is an increased secretion of the cutaneous glands, so that the skin becomes moist and greasy, and shows a tendency to hyper-trichosis, while, according to Cushing, in hypo-pituitarism the skin is smooth and free from moisture.

I have not so far seen any account of the employment of pituitary extract in ichthyosis, but it is probably worthy of a trial to stimulate the cutaneous glands, if they are still present, and so counteract the excessive dryness of the skin. In any but the mildest cases of ichthyosis, this would be useless, for there is both an anhydrosis and an asteatosis, owing to an atrophy of the sebaceous glands and changes in the sweat coils which interfere with their functioning.

THYMUS GLAND.

So far no definite relationship has been established between cutaneous disorders and absence or disease of the thymus gland. It is worthy of note, however, that the thymus as a rule becomes functionless about puberty, and that at this time there is an increased growth of hair, a tendency to the development of acne vulgaris, the scalp becomes an unsuitable soil for the growth of the microsporon fungus of ringworm, and juvenile warts tend to disappear spontaneously. It has been suggested that it is the thymic secretion which renders the skin susceptible to the ringworm fungus, and inhibits the sexual development with its associated hair growth, and that possibly thymus extract might have some influence in reducing the tendency to comedones, and be of benefit in acne vulgaris.

OVARIES AND TESTICLES.

It is not improbable that the hormones secreted by the ovaries and testicles may exert an influence on the skin,

especially with regard to the hair growth. With the development of the sexual organs, there is a marked growth of hair, but as the sexual development increases it is not infrequently associated with premature baldness in men, while, according to Sabouraud, eunuchs are rarely if ever bald. In women, the cessation of the sexual function at the menopause may correspond to an excessive hair growth on the face, and about the same time certain cutaneous diseases of supposed nervous origin, such as lichen planus, flushing, or attacks of pruritus, are liable to supervene, and more rarely dermatitis herpetiformis, attacks of psoriasis, or outbreaks of eczema in an individual subject to them. The possibility of benefiting such conditions by organo-therapy is worthy of consideration and experiment.

The whole subject of the relation of the internal secretions to the skin is one of profound interest, and opens up possibilities with regard to the ætiology of certain cutaneous affections, the cause of which is at present obscure. It is not improbable that, in the near future, organo-therapy may come to play a much more important part in the treatment of these diseases than it has done in the past.

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INTERNAL SECRETIONS AND THE PSYCHOSES.

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THE rôle of the internal secretions in their causal, coincidental, and sequential relationships to mental disorders has already received a considerable amount of attention. In connection with the thyroid, the parathyroids, the epithelial layer of the suprarenals, the glandular portion of the hypophysis cerebri (pituitary gland), and the inter-tubular cell-agglomerations of the pancreas, much has been written and many clinical phenomena noted. With regard to the positive excrementitial glandular secretions (the production of hormones) much evidence has accumulated; so also with regard to the negative secretions which are concerned with the neutratization of materials circulating in the blood we now possess data of great interest. It must be confessed, however, that with regard to the excrementitial secretions and the rôle they play in the bodily economy when they are but imperfectly excreted there is still scope for much investigation and further elaboration. Particularly so is this the case in connection with the functions of the genital glands in the production of semen and in the release of ova.

In considering the functions of the internal secretions, it would appear to be important to recognize that in order that the functions of the bodily mechanism may be adequately maintained, the balance of the internal secretions should also be adequate and unimpaired; that is to say, each of the several secretions should be regarded from the point of view of its adequacy, either in its normal or in its diminished or increased (compensatory) proportionate relationships to the other internal secretions. Thus, were we warranted in assuming the existence of a quartet or quintet of hormones interdependent upon each other for bodily harmony, it would

not be in itself sufficient to establish the facts of the existence of a diminution or excess of this or that secretion unless we also sought to determine the effect of such diminution or excess upon the relative amounts of the other internal secretions called forth or necessitated thereby.

In connection with the excrementitial secretions and the possibility of their retention in the bodily economy, many important and difficult considerations arise and the study of the rôle of the genital glands presents difficulties which require a vast amount of careful investigation for their elucidation.

In approaching this subject of the interrelationships of the various hormones, it would appear advisable, therefore, to do so on a similar principle to the Jacksonian with regard to convulsions and to recognize that not only may there exist a functional increase or diminution of one type of hormones, but also a relative or compensatory increase or diminution of the secretion of one or several of the undamaged remainder. That this mutual interdependence does exist in very complex modes is evidenced in many ways in connection with the recrementitial secretions, and there are many data which suggest that diminution or excess in the production of the secretions of the genital glands attended by their undue retention or excretion may also affect the balance of the recrementitial secretions. It is obvious that it is not yet possible to make a sharp division between the two categories of glands; but it is warrantable to assume that a lesion of any important gland makes itself felt throughout the whole of the chemical interchange of the body and that a state of endogenous or auto-intoxication may be induced thereby.

That the nervous system is becoming more prone to suffer from defects in the internal secretory mechanism as the stress of civilization increases, is a fact which is becoming more and more manifest. Just as the more highly evolved nervous structures coincidental to a higher civilization have become more highly evolved and less stable, and therefore more liable to suffer from the effects of toxins from without, so also do they tend to be more readily disturbed by auto-toxins engendered from within, and even by comparatively slight variations in the balance between the various hormones. This is exemplified over and over again in connection with recurring

and alternating psychoses, and much evidence goes to show that their periodicity is due to rhythmical variations in the production and elimination of the various secretions.

Thyro-parathyroid Affections.—The thyroid and the parathyroid apparatuses have received much attention by psychiatrists, but, pending more satisfactory agreement as to the mode of action and the difference between the function of the thyroid and the parathyroids, there is yet much investigation to be carried out. The trophic functions of the thyroid and the anti-toxic functions claimed for the parathyroid secretions, although closely allied, are nevertheless regarded by some as specifically distinct. Whether this claim is warranted, or that the chemical trophic action of the one is nothing more than an anti-toxic action neutralizing some poisons of less virulence than are neutralized by the more specifically antitoxic role of the other is yet a matter for elucidation. That both these secretions are necessary for the adequate elimination of nitrogenous products of metabolism by the kidneys has been proved by the researches of Coronedi, and perversions of the thyro-parathyroid apparatus are apt to be followed by renal insufficiency and disease.

Functional insufficiency of the thyroid gland is followed by the morbid syndrome, endemic cretinism. It is well known that similar groups of mental, and sometimes physical, symptoms follow insufficiency of thyroid activity. In sporadic cretinism, in which the thyroid is injured or destroyed in earliest infancy, the effects may be even more marked. Besides the torpor and myxœdema, there may be an arrest of the development of both body and mind, which can, however, if taken at a sufficiently early period, be modified or even rapidly overcome by the administration by the mouth of either fresh or dried thyroid. The causes of the changes in the thyroid are as yet insufficiently known.

The somatic evidences of cretinism are well known and are dealt with elsewhere. The psychical evidences may be characterized as a mass of defects, but there are certain features which differentiate the condition from other types of arrest. As in other forms of athyroidism, torpor and slowness of mental reaction are characteristic. Psychical development is arrested, although there is some degree of intelligence.

The emotional faculties are dull and but seldom are there any true perversions of the emotions or impulsive tendencies. It is customary to distinguish three classes—cretins, semi-cretins, and cretinoids. True cretins are usually idiots. The other types are mentally deficient or simple-minded. In the more severe cases speech is imperfect, and although bodily development is capable of improvement under treatment, the same cannot always be said of the mind. If the cretinism be less severe, the individuals may sometimes be educated so as to fulfil certain social necessities. Emotionally, although usually placid and unmoved, they may evince evidences of fear, affection, etc. Volition is imperfect and delayed owing to lack of initiative and difficulty of acting with energy. The sense of sight, and even the colour sense, is usually normal. Hearing, however, is frequently very defective, as are also the senses of smell, touch, and muscular movement.

Myxœdema.—In the myxœdema of adults which follows grave lesions of the thyroid either from disease or resection, there is a characteristic mental torpor. According to Brissaud, there is a fundamental difference between myxœdema and infantilism (due to a thyroid lesion) and psychical arrest and idiocy (dependent on a lesion of the parathyroid). Tanzi recognizes a considerable variety of intermediate forms between the myxœdematous infantilism of Brissaud and the more severe degree of sporadic cretinism, and, excluding the cases in which the parathyroids are present and uninjured, there exist extreme degrees of dwarfing, infantilism and brady-trophism which are never unaccompanied by psychical disturbances. There is always a slight degree of psychical infantilism, and the apathy, sluggishness, and excessive seriousness of character bear witness, if not directly to athyroidism, at least to the brady-trophism which is the result of athyroidism.

In addition to the physical characteristics of myxœdema, the mental symptoms are gentleness, placidity, indifference, and only occasional ruffling of the temper. There is slowness of thought and action. Sometimes there is excessive somnolence, especially in the daytime (Savage). Hallucinations and delusions are frequent. When insanity occurs the

symptoms are usually subacute and may be those of mania, melancholia or dementia. Memory is usually impaired. Insanity with myxœdema occurs chiefly in middle-aged women and not infrequently their delusions are connected with the sense of disfigurement due to the disease. In most instances known to the writer the condition has yielded readily to appropriate treatment by thyroid extract.

Exophthalmic Goitre due to hyper- or dys-function of the thyroid gland is not infrequently associated with insanity, which may range from simple melancholia to acute mania. The most recent investigations show that even if there is hyperactivity of the thyroid, there is in all probability also a lesion and a functional insufficiency of the parathyroids. Tanzi refers to a characteristic and constant psychical syndrome consisting in excitement, restlessness, anxiety, loss of memory, and indecision of will. To these he also adds doubts of an obsessive nature, preoccupations, irresolution, incapability of mental work, irritability, diffidence, omens, and timidity. Sometimes such patients suddenly lose power over their muscles, and fall to the ground (*effrondrement des jambes*), or allow objects which they hold in their hands to slip through them. The prognosis is largely dependent on that for the exophthalmic goitre. The treatment is mainly that for the exophthalmic goitre. The writer has obtained fairly good results by the aid of careful massage of the regions surrounding the thyroid, performed with a view to facilitating the lymphatic and venous flow from the gland. Savage has noted in these cases the tendency to periodicity, there being alternations between disorder and health, and between excitement and depression. General paralysis in association with exophthalmic goitre has also been noted in connection with parathyroid functional insufficiency, we have to note the occurrence of paralysis agitans, tetany, myoclonic epilepsy and mytonia, whilst with hyper- or dys- function myasthenia pseudo-paralytica and mytonia periodica occur.

Suprarenal Capsules.—Of late the subject of suprarenal glandular efficiency has assumed some importance in psychiatry. The effects of variations in internal secretion of adrenalin in the production of arterio-sclerosis and arterial hypertension must of necessity have considerable bearing on the various problems of the brain and mind. Suprarenal insufficiency is

apt to be attended by lassitude, fatigue, and possibly also by increased toxicity of the viscera and of the urine. It is also assumed from the findings of Strehl, Weiss, Soddu, Charrin and Langlois that the suprarenals help to render innocuous certain toxic products of metabolism. That suppression of the suprarenal function is followed by nervous and mental troubles is evidenced by many observers. Weigert, Lomer and Zander refer to hypoplasia of the suprarenals as of frequent occurrence in certain disturbances in the embryological development of the brain, more especially in anencephaly and hemicephaly. Zander refers to a reduction in the size of the suprarenals in cases where, at a certain stage of embryonic development, the anterior portions of the cerebral hemispheres have perished. Czermy found in five cases of congenital hydrocephalus complete absence of the medullary substance of the suprarenals, the cortex remaining intact. That the suprarenal system will come into greater prominence in the consideration of various nervous disorders is probable, and there are already indications that not only is the sympathetic nervous system in close co-operation with the suprarenal system, but also that the co-operation may have some bearing on the production of the various endo-cellular hydrotic phenomena so characteristic throughout a wide range of nervous phenomena extending from occupation spasms and choreas to epilepsy and hydrocephalus.

The Pituitary Gland.—The hypophysis cerebri has been regarded as an internal secretory organ from earliest times, and the relationships of its functional variations to developmental and epileptic states have been the subject of some speculation by Wenzel, Brown-Séquard, Marie and others. Much interest has centred round the question as to whether the nervous portion of the hypophysis contains nerve cells. True nerve cells and nerve fibres are said to occur (Krause, Berkley, Ramon y Cajal). Other observers (Kölliker, Caselli and others) believe that the cell elements are glial and ependymal rather than truly nervous.

The colloid secretion, and its rôle in the bodily economy, is still a matter for investigation, and the views concerning the results of hypophysectomy are so contradictory that it is as yet too early to formulate conclusions. Similarly, with regard to

the hypertensive action of pituitary extract further elucidation is needed.

The somatic symptoms of acromegaly are generally accompanied by lassitude, muscular pain, progressive apathy and morbid somnolence. The sexual functions usually diminish in activity. When there are symptoms such as headache, giddiness, vomiting, failing intelligence and somnolence there may be an actual cerebral tumour present. That there are many important relationships between the sexual glands and the hypophysis has been demonstrated by Launois and Mulon, and Thaon in connection with pregnancy and lactation; by Fichera, in relation to the ovary; and by Rössle, with regard to the testicles, ovaries, and the uterus.

That there are many complex relationships between the sexual secretory functions and hypophysal obesity (dystrophia adiposogenitalis or Froelich's syndrome) there can be no doubt, and we may look to the future for many interesting revelations as to the rôle of the interactions of these internal secretions in the production of dementia præcox, and other developmental morbid mental states.

THYROID INSUFFICIENCY IN GENERAL PRACTICE.

By J. PARLANE GRANGER, F.R.C.S.

[With Plates XXXV–XXXVIII.]

In the address on Medicine, delivered at the 81st Annual Meeting of the British Medical Association, Professor George Murray drew attention to one of his cases in which enlargement and induration of the thyroid gland were arrested before the onset of complete functional inactivity. He then proceeded: "It is possible, although actual proof is still lacking, that in some of these cases the surviving portion of the gland may after a time, by a process of compensatory hypertrophy, be able to supply a sufficient amount of secretion to remove symptoms. In order to settle this question, careful observations continued for a long period are required so as to ascertain if a slight case of myxœdema ever does recover spontaneously, or if, after the symptoms have been removed by treatment, it is possible for the patient to remain in health when the treatment is stopped." He added: "It is to those engaged in general practice that we must look for a solution of this and other similar interesting clinical problems."

In this article an endeavour will be made, though perhaps in a modest way, to discover an answer to the problem which Dr. Murray has set. I do not, however, intend to confine my attention to this alone, for that would restrict the scope of the article within limits that its title does not endorse.

The practitioner may legitimately regard the whole history of a disease as his peculiar province. He need not be too scientific, so long as he can cure his patient. The pleasure and satisfaction of confirming a diagnosis by *post-mortem* examination may safely be left to the pathologist. To the practitioner, a living patient is better than a dead pathological curiosity. In general practice, too, the personal equation looms large, for in this, the Art of Medicine conforms to Zola's definition of

Art as "Nature seen athwart a temperament." Clinical material is sometimes all the better for the shadow of individualism lying across the bed, especially when that shadow bears with it a sprinkling of anatomy, a little physiology, the sidelight of history, and some reasoning, inductive, deductive, or both, according as the cases act and re-act upon the mind, coloured, as the practitioner's must be, by reading, methods, and results; particularly the results, for response to treatment is his guide to correct a faulty diagnosis.

This disease is not one about which Hippocrates wrote, nor indeed, so far as is known, any of the Greek or Roman practitioners. Paracelsus, the chemical physician, was the first to give a trustworthy account of cretinism, and to point out its association with goitre. This treatise was written in the early part of the 17th century, and Hirsch, commenting upon it, says: "Before this, as regards cretinism, its history is involved in complete obscurity."[1] Cretinism was the only form of thyroid insufficiency known, before Sir Wm. Gull published his paper, "On a cretinoid condition supervening in adult women," in 1874. Who first suggested the phrase "Thyroid insufficiency," I have never been able to discover.[2]

In many of the cases in adults I have had under treatment, thyroid insufficiency has been a subsequent development to an hyper-thyroidism occurring over a more or less prolonged period. It is not, therefore, straining the premises too severely to conclude, that the vicious circle of to-day was the vicious circle of yesterday, and that thyroid insufficiency, cretinism, and myxœdema, although all of comparatively modern nomenclature, must refer to conditions of unhealth as old as goitre itself.

Now, although the Greeks knew not goitre and the Roman physicians wrote no treatises on it, historians, poets, and, later, churchmen and travellers of that Empire, left quite distinct records of the disease; even more interesting is their naming the places where the disease is found endemic to-day. Vitruvius writes "The neck of man is frequently found to be swollen among the inhabitants of Maurienne and the Middle

[1] *Geographical and Historical Pathology*, by August Hirsch, p. 121.

[2] It was Dr. Léopold-Lévi, from whose pen an article appears in this issue, commencing at page 199. [Ed.]

Alps."[1] Juvenal calls attention to this "guttur tumidum" and adds "this swelling of the neck is found among the Alps."[2] Ovid, in the Fasti, refers to the slight swelling of the neck that occurs in the first months of pregnancy, a condition with which we are all familiar, which, no doubt, is due to the general disturbance among the endocrinic glands caused by the cessation of ovulation, and the interdependence of the hormonal contents of these glands. Pliny even goes the length of blaming "the water which is drunk,"[3] a very shrewd guess in view of the now well ascertained fact that there are undoubted goitre-producing wells in these regions. If, therefore, the assumption be correct, that wherever goitre exists, there also will thyroid insufficiency be found, this condition of unhealth must be possessed of quite a hoary antiquity.

Its wide-flung ramifications are equally remarkable. Marco Paola, in his journey to China early in the 14th century, saw and remarked upon the prevalence of goitre in Yarkand and the Central Asian plateau. Humboldt found it prevalent in the Cordilleras of the New World, and Mungo Park gives an account of it as occurring in the Cong Mountains and upper basin of the Niger.

Although the intimate association of cretinism with goitre was well known in the early part of the 17th century, owing to the works of Paracelsus, its true pathological significance was not known until a much later date. That a cretinoid condition could develop in an adult did not dawn upon the medical world until 1874, when Sir Wm. Gull published his five cases, all of them being adult women. It was not until 13 years later (1887), when Dr. Savill published a paper in the *British Medical Journal*, in which he recorded the disease as occurring in a male subject, that medical knowledge advanced another step, and rose to the conception of this disease being common to both sexes.

Dr. Ord, in a paper published in the *Medico-Chirurgical Transactions* (1878, p. 43), christened this cretinoid condition

[1] Vitruvius: *De Architectura*, Vol. I., p. 220, "Guttur homini intumescit præsertim apud Aequicolas et Medullos Alpinos."

[2] Juvenal: *Satyr.* 13, "Ovris tumidum guttur miratur in Alpibus."

[3] Pliny: *Hist. Natural*, lib. IX., cap. 37, "Guttur homini tantum et suibus intumescit, aquarum quæ potantur plerumque vitio."

in adults by the name of myxœdema (myxa = *mucus*, oidema = *swelling*). He believed that the swelling was due to a mucoid infiltration of the deeper layers of the corium. This point is still in doubt. Swale Vincent, who may be regarded as having said the last word on this subject, writes: "The chemical nature of the infiltration is not certainly known. It is very doubtful whether it is mucin, and there are many reasons for thinking that it has not the composition of true œdema. Cases in which a chemical examination of the skin can be carried out are so rare, that it will probably be many years before the matter can be satisfactorily settled."[1]

The association of myxœdema with thyroid atrophy was first clearly established at the International Medical Congress held at Copenhagen in 1886. After the close of the congress, the Clinical Society of London appointed a committee, subsequently named the "Myxœdema Committee," to investigate the whole matter thoroughly. This committee published their report in 1888, which completely confirmed the paper on the ætiology of this disease read by Dr. Hadden at the Copenhagen Congress two years before. In 15 of the cases investigated by this committee, the thyroid was examined *post mortem*, and in every one it was found diminished in size, and showed atrophic and other degenerative changes.

In 1889, the year following the publication of this report, I saw, in the wards of the Glasgow Royal Infirmary, a case of myxœdema for the first time. The patient was an adult woman, and was only there for demonstration purposes; having fulfilled this function, she was dismissed the wards without treatment of any kind. I never forgot that case, and it was the means of focussing my attention upon thyroid troubles at a very early period in my medical career.

Just about this time, Brown-Séquard's experiments upon himself with testicular extract were much talked about. To many, this was only an *affaire pour rire;* but it attracted the attention of the medical world to the possibilities of organotherapy, and, no doubt, influenced Dr. Geo. Murray to try an extract prepared from the healthy thyroid of an animal upon a case of myxœdema under his care. He made an

[1] *Internal Secretions and the Ductless Glands*, (pub. 1912) by Swale Vincent, p. 278

extract from the thyroid of a newly killed sheep, and used it with good results. That preparation is now the Liquor Thyroidei, P.B. Dr. Murray described this case and its treatment at the Annual Meeting of the British Medical Association in 1891. In July of last year, he again reported on it. The patient was then alive and well, and was kept in good health by the daily ingestion of 10 m. of the extract. Other experimenters found that equally good results were achieved by feeding the patients with thyroid gland substance.

It was thus that thyroid therapy began. Not even its nimble-witted pioneers had any idea of the immensity of the new fields they had discovered. Desiccated thyroid was too important a therapeutic agent to confine within the narrow limits of its discoverers. Men began to use it in all sorts and varieties of ill-health, and met with astonishing results in cases that bore no resemblance whatever to myxœdema. The physiological content of the gland had no meaning, when it was confronted with the variety and diversity of the symptoms, that sometimes cleared up like mists before the sun when thyroid was administered. Burroughs Wellcome & Co. placed the "Tabloid" Thyroid Gland upon the market in 1894. This did not contain an extract, but a dried preparation of the whole gland substance. When Baumann, in 1896, pointed out that the chief ingredient of thyroid secretion was an organic iodide, this firm standardized their thyroid preparations, so that to-day each product represents a definite amount, and contains not less than 0·2 per cent. of iodine in organic combination. This is important. I have tried the dried thyroid of the Pharmacopœia, but it varies so much that, if one desires to get the best and speediest result of treatment, it is necessary to use either the "tabloid" thyroid gland, or some other standardized preparation.

It was just after these tabloids had been placed upon the market, that I made the diagnosis of thyroid insufficiency for the first time in private practice. A middle-aged woman had brought to my rooms a daughter suffering from a simple dyspeptic trouble, and seeing her daughter's pains speedily vanish, said "I wish you could do something for me." The woman was about 55 years of age, pale visaged and *petite*. The eyes were clear and dark, and looked out upon the world

through narrowed lids. From each lower lid was suspended a blue-red, beefy swelling, about the size of a filbert. These swellings stood out in marked relief upon a face otherwise absolutely pallid, and gave to the whole countenance an ugly and repulsive look. The upper lids were swollen as well, but the swelling was slight and pale. There were no other swellings about the body. She told me she was so depressed that she had to compel herself to do the necessary work of the house, and that other things had to be left. In addition to this great bodily weakness, her appearance was such that she dared not stir abroad, except in the dusk of the evening, and for this reason had been unable to go to any public place of amusement for some years. Her condition was as miserable as it well could be. Fifty-five years of age and the mother of a grown up family, she had arrived at the time of life when her early struggles and sacrifices entitled her to that greater ease and comfort, which a grown-up family generally assures to the parents of the working classes.

I had never before seen anything to resemble these blue-red, beefy swellings; indeed, I have never since seen anything like them. Œdematous swelling of the eyelids is one of the commonest signs of thyroid scarcity; but that is pale and alabaster-like; in typical cases, one seems to see right beneath the surface. However, the narrowed palpebral clefts and the pale œdematous swelling of the upper lids, although there was no œdema in any other part of the body—called to mind some resemblance in the myxœdematous case I had seen in the wards five years earlier. Hesitatingly and without much hope, I prescribed for her, giving her one 5-gr. thyroid tabloid each night, and a mixture containing sulphate of soda, and ordered a diet largely composed of proteids, limiting the starches to thin crisp toast. No fluids were allowed with the meals.

The use of accessory drugs with thyroid is contrary to what has been advised, but I do not agree with this. I have tried both ways, and I have no hesitation in saying that the well-being of the patient is not only hastened but intensified by taking other drugs, concurrently with the thyroid, at least in the early stages of treatment, and particularly in those

cases complicated with obesity, as many of them are. In children the combination of thyroid extract with gr. ½ of Hyd. c. Cret., and small doses of Syr. Ferri Iodid. after meals, I have found to be a very useful prescription.

The result of the treatment of the above case was beyond all expectation. In the short space of three weeks, the blue-red, pendulous swelling of the lower lids had almost gone. Vigour and health rapidly returned, and in six weeks, to her own very great pleasure and my delight, she declared herself perfectly well. I am not sure whether the patient or the practitioner was the better pleased of the two. Certainly to myself this case was a great revelation. It was the beginning of thyroid therapy in my own practice, and the treatment was thereafter largely used by me, experimentally, in many conditions of unhealth, lying outside the run of the well-known types of disease named and discussed in text-books.

The second case, I wish to record, occurred during my early and tentative gropings after results with thyroid therapy, and is that of a boy, four years of age. As he sat on his mother's knee, his head hung forward so that the chin rested on the thorax, the lips were thickened, and saliva dribbled from the mouth. The palpebral clefts were narrowed, and the face was quite expressionless. His hair was thin and dry, and he took no notice of anything.

On stripping, I found him emaciated in a high degree. His legs and arms were like pipe-stems, and the dry, withered skin hung loosely over the bones. His spine was arched like a bow; the chest was an irregular rhomboid, and the ribs presented the rosary of rickets in perfection. His belly was the biggest thing about him, being large, round, and tympanitic. His appearance suggested that he was a cretin, but I had never seen one. In the books it was stated that the disease was extinct in Britain, and on the strength of legitimate authority the case was, presumably, a very severe form of rickets. However, having seen and read descriptions of this Alpine disease, and being in the first stage of my enthusiasm for thyroid, I resolved to try it. I gave him ½ gr. of Hyd. c. Cret., and a 2 gr. thyroid tabloid each night, and 20 m. of Syr. Ferri Iodid. t.i.d. The child almost immediately began to get well. His limbs filled out, his abdomen became reduced in size, and

he began to sit up and take an interest in things. In six weeks, he began to walk.

This patient afterwards became quite a healthy child, and the last time I visited his parents' house I was told he was well and at regular work. To my knowledge, he has never again required thyroid treatment. That point is interesting, and I shall deal with it later.

At that time, the phrases thyroid therapy and thyroid insufficiency had not been coined. Yet practitioners all over the country must have been using the drug and getting results, for in the late nineties, in conversation with Dr. Cullen Brown of Alexandria, after a consultation, he asked if I had ever tried thyroid gland in the obesity of the menopause. On comparing notes, we found that we were both using this medication empirically in certain irregular cases, and getting occasional results. To neither of us had it occurred that we were dealing with hyperplasias and partial atrophies of the thyroid gland, the residuary legatee of the toxæmias of other diseases, apparently long since recovered from. There was, indeed some excuse for this empiricism on the part of practitioners. The association of myxœdema with thyroid starvation, and its occurrence about the time of the menopause or later—cretinism being practically unknown in the west of Scotland—helped to fix the mind of practitioners in these parts upon the later stages of life as the time for the occurrence of thyroid insufficiency. The facts are, nevertheless, rather the reverse, for the whole gamut of the years of man is susceptible to adversities from this cause, and the years of childhood most of all. At the two extremities of life, we have cretinism on the one hand and myxœdema on the other, both associated with an absolute, or nearly absolute, deprivation of thyroid secretion from the system.

There is nothing comparable in the symptoms of these two diseases. Both in age and symptomatic exhibition they are far apart, and no one, from the association of ideas called forth by similitude of symptoms, would for one moment think of ascribing to these two diseases a common cause. Yet such is the case, and I call attention to this now to show how varied, how unusual, and how antagonistic even, conditions and symptoms may be when the human system is operated

on by the same pathological factor; provided that factor is thyroid secretion in any of its abnormal developments, whether excess, total deprivation, scarcity, or alteration of its chemical contents.

The third case to which I wish to draw attention is that of Mrs. M. (Figs. 1 and 2, Plate XXXV.), whose history I will give in her own words:—

Married in March 1898. Had good health till about the beginning of 1899, when I contracted kidney trouble, and was treated by Dr. S. for Bright's disease. In about a year I was completely cured.

In September, 1900, my child was born, and I believe he was a healthy boy, but he developed convulsions when he was 8 months old, and died on 23rd May 1901. A month afterwards, my father died suddenly, and no doubt the grief for the loss of my child and my parent caused me to get low-spirited, and I began to feel my health giving way. I felt about that time that I had not sufficient strength or energy to do my ordinary household duties, was despondent and irritable and could not make myself interested in anything. Could not be bothered even to read.

In August, 1902, I was on holiday at Callander, and at that time was 6 months pregnant. Whether I had over-exerted myself or not I cannot say, but I gave birth to a living child then; I remained in Callander a fortnight after the birth. When I got home, I was far from well, and I had to take to my bed. Up to this time I had not thought there was anything very seriously the matter with me, but I now began to think I had some disease.

Previous to my marriage I earned my living by singing—I was a professional vocalist—but I now found my voice was getting husky, and I suffered from shortness of breath. I also had fainting turns, and felt at times that I was losing the power of my legs. On one occasion, I had rather a severe attack of this numbness in my legs, and I collapsed altogether. My neighbour called in Dr. B., and he said my nerves were out of order.

At this time I should say I had much trouble at my periods, and there was always an excessive flooding, which lasted sometimes for a week and 10 days. This was a matter of great concern to me, and worried me terribly. It got gradually worse.

Nearly the whole of 1903 I attended Dr. M. for my voice, but his treatment had absolutely no effect. My trouble in this direction really got worse rather than better, and because of this and the fact that my periods were still causing trouble, I again put myself into Dr. B.'s hands, and shortly afterwards again became pregnant.

At 6 months there was a miscarriage, and still the trouble remained. Dr. B. cauterized the womb without effect, and ultimately he advised me to undergo an operation. This operation, which I think was called "curetting," was performed by Dr. K. I think this operation took place in March, 1906.

I was still occasionally troubled with these floodings and my other troubles were as acute as before. My face was swollen out of shape, so

were my hands and feet and also my legs. My voice was completely gone, and when it came back at intervals I had great difficulty in articulating. The numbness also continued, legs particularly. My complexion was ghastly, and people who knew me very well passed me in the street at times not knowing me. My hands and feet were always like ice. Up till this time (1908) things went on just as described, and I had really come to think that so long as I got no worse I should be thankful, but it never occurred to me that I would ever be better. In October of this year I met Dr. G. in my mother-in-law's house, and after having a conversation with him I decided to place myself in his hands. He prescribed a certain treatment, and almost immediately I began to feel an improvement. The swelling began gradually to disappear. I got to feel that my household duties interested me, for I could perform them with some degree of pleasure and without any fatigue. My voice gradually came back, and in the winter of 1909 I sang again in public without a trace of any weakness or unreliability in my voice. Realizing the improvement I got quite cheerful, entering into company in a quiet way as before the trouble, and sang at various small concerts.

In March, 1909, I went to a dance, and danced all the dances. I became pregnant again about then, and in November a healthy child was born. She is still a healthy child, and my own health never was better in all my life.

The clinical history of Mrs. M., beginning as it does in the year 1901 and extending to her recovery in 1910, covers a period of 10 years. It is particularly interesting, not only because of the perfect relief which thyroid therapy brought, but because it exhibits, within the compass of a single life, the wide ramifications of unhealth that can be caused by thyroid insufficiency. In the second place, we have here the history of a type. During the early years of her illness, hyperthyroidism and not insufficiency was the prevailing condition. Mrs. M. was one of those cases of goitre that show very little or no enlargement of the gland throughout the whole course of the disease. Such an absence of enlargement is not at all uncommon in the early stages of exophthalmic goitre; indeed, in nearly every case which I have seen, the rapid pulse, the palpitations, the flushed face, and sometimes even the prominent eyes have preceded the thyroid enlargement by a period of months.

In other cases, and Mrs. M. is one of these, no enlargement takes place at any period of the disease. It may be asked whether this case was not one of insufficiency from the first. Her report omits one item of importance to this thought, which is, that when she came from Clydebank to

Fig. 1.—*Photo of Mrs. M. taken in 1907, one year before commencement of thyroid treatment.*

Fig. 2.—*Photo of Mrs. M. taken in 1914, two years after treatment had been stopped.*

See p. 325 for clinical history.

Fig. 3. *Mrs. A., aged* [illegible] *years. Neck band,* 19½ *inches. Photo was taken in 8th year of her illness.*

Fig. 4. *Mrs. A., aged* 61 *years. Neck band,* 14 *inches. This photo was taken* 8 *years after No.* [illegible]

For clinical history, see p. 332.

Glasgow I was the first doctor called in, and she was my patient for a year. I tried iron, arsenic, strychnia, bromides, rest in bed, dieting, change of air, and all with no effect. Then finding no thyroid enlargement, and at the same time observing the flushed cheek and the injected vessels over the malar bones, so common an accompaniment of insufficiency before the onset of myxœdema, I resolved as a counsel of despair to administer thyroid.

If thyroid is going to do any good, the response is more or or less immediate. One week's tentative trial, in many cases, a few days, will serve to clear up the diagnosis. In her case, the symptoms were aggravated rather than improved; consequently, my first diagnosis, to wit, hyperthyroidism, or some alteration of the chemical content of the gland, was proven. We have then, in this case, excessive thyroid activity passing gradually to that degree of atrophy in which the early signs of myxœdema were developed, the whole cycle of changes being counted by a term of six years. (1901—beginning of illness; 1907, first sign of myxœdematous swelling.) This cycle, from excess to deprivation, is not only peculiar to this type, but the six years occupied in the process are a fair average of the time it takes to do it.

The next point, I wish to make, is the large number of important systems involved. Books lay much stress upon the skin and its appendages as the favourite seat of the manifestations of thyroid disease, and perhaps rightly so. But in this case metabolism was disturbed, and function altered in nearly every department of the organism, long before the onset of myxœdema. Taking the voice, to begin with, the patient was a professional singer, and took much pride in this accomplishment. Both she and her husband regarded her singing voice as a valuable asset. This is proved by her attending a throat specialist for a whole year, at a time when the pernicious influence of this disease had so prostrated her physical powers, that it was difficult for her to carry out her more immediate duties in the house.

Not only did her voice lose tone, but its range was seriously impaired as well, especially in the higher notes, two of which were completely lost. Within a few weeks of taking thyroid her high notes were recaptured, and her voice is now

as good as ever.

This effect of thyroid insufficiency upon the singing voice is not well known. I am not now dealing with the slow and laboured speech of typical myxœdema. Mrs. M. had not reached that stage. I have never seen this symptom mentioned in books, and the throat specialist, whom she attended for a year, if aware of it, did not in this case suspect it. Dr. Dundas Grant wrote an article,[1] about three months ago, on the various causes of defect in the singing voice. He tabulated over 100 different causes, but I looked in vain among these for thyroid insufficiency, although thyroid enlargement was mentioned as a mechanical interference.

The next system to be involved was the menstrual cycle. She suffered from irregularities in the flow, and it was always excessive. This condition existed not merely during the period of hyperthyroidism, but during her thyroid scarcity as well. It was present from the beginning of her illness in 1901, and remained with her till her cure in 1910. During these years, apart from other treatment, one of the leading gynæcologists in this city was called in consultation, and recommended curettage of the womb. His advice was followed, he himself performing the operation, but after the operation the old irregularity was maintained.

Then again, this disease coloured her motherhood. During these years of illness, three times she became pregnant, and, notwithstanding every care, each separate time she suffered miscarriage. She abandoned all hope of being a mother. After treatment with the thyroid gland, she again fell with child, and this time she kept well throughout, had a natural confinement, and gave birth to a healthy baby girl, who is alive and well at the present time. It is evident, therefore, what an important force thyroid secretion exerts upon the well-being of the organs of sex and the function of motherhood. Being very desirous of achieving this crowning glory of a woman's life, it was a fortunate thing for my patient that her full sexual development was completed before the onset of thyroid insufficiency. A healthy thyroid is almost necessary

[1] *Clinical Journal*, November, 1913, pp. 481 and 503. The exact number of causes catalogued was 173.

to the full and perfect development of the organs of sex; just as excess of pituitrin in children may bring about precocity, so insufficiency of thyroid delays development.

How many young married women it has fallen to the lot of every practitioner to examine, because the years have passed, and no child has come to bless the mating. On examination, we find the uterus is infantile, and the patient has to be sent sorrowfully away. Many of these cases, I am not sure whether I might not be within the compass of truth in saying nearly all, have their thyroids to blame for the infantilism.

Unfortunately, the treatment to be successful, must be begun early. We are dealing with development here, and not with altered function; so that the treatment to be successful must be initiated during the developmental period. After the 21st year, the treatment of infantilism is practically hopeless. One of the strange things is that while the thyroid scarcity may be sufficient to delay developmental changes at puberty, few, if any other, symptoms may be present.

Another case I can quote bears this out. To all outward appearance, the patient was a perfectly healthy young woman, and, what is more, she felt well. She went regularly to a mill, and felt fit and able to do her work there. She was 19 years of age in May 1914. She first menstruated in her 15th year, since which time the flow has come at rare and long intervals, and then insufficient in amount. For instance, she menstruated in July 1913, and not again until after an interval of seven months. She never suffered from anæmia, had never been off work, and never felt unwell. I did not examine the womb to see if it was infantile. Some symptoms, however, to a specialist in symptoms, as all practitioners of many years standing are, when considered in the light of our experience and acquired knowledge, are as important and informative as physical signs.

This young woman was evidently in perfect health but for one thing. During the most important five years of her sexual development, the monthly period has only appeared at rare and long intervals. In the light of my experience of 24 years, that condition of things, taken in association with her otherwise perfect health, points to but one thing, and that is an imperfect development of the organs of sex,

which, if allowed to proceed, will inevitably result in infantilism.

Well, one cannot always be on the watch, and it is perhaps as well. For over four months, I treated her with iron and arsenic, hot hip baths, sinapisms, and the usual routine treatment for amenorrhœa. Each time she returned with the same story of feeling perfectly well, but she never menstruated. It then occurred to me that I was dealing with a case of imperfect development, and I prescribed for her: Tab. Thyroid Gland grs. iij, Hyd. c. Cret. gr. i, Pulv. Rhei gr. ij. Fiat pulv.

One powder to be taken each night at bed-time.

In three weeks menstruation occurred, normal in amount and without pain, and she still continues to be regular.

Returning again to Mrs. M., the next system we find involved is the skin and its appendages. If her own report is consulted, it will be found that she first noticed the thickening of the skin, which is so characteristic of the later stages of the disease, 1906 and 1908. It is as though one had run a fine, semi-elastic cement into the deeper layers of the corium, the swelling making the whole body stiff, and rendering every movement laborious. I have already given Dr. Ord's opinion of its nature, and Swale Vincent's commentary thereon, but its clinical manifestations are of more importance. When fully developed, it is uniform over the whole body, and is neither varied nor worsened by position or movement. It does not pit on pressure. It usually occurs first upon the face, especially about the eyelids, the chin, and the malar bones; the eyelids are particularly affected, and become swollen with a solid, wrinkled œdema, which produces a characteristic narrowing of the palpebral clefts.

In other cases, this œdematous swelling becomes pendulous, especially about the breasts in males. A male patient (Fig. 5, Plate XXXVII.), still under treatment, had breasts which were pendulous to the extent of three inches, when I saw him first, two years ago. In early cases, especially in fair-haired people, the œdema is almost transparent, but when punctured with a needle, no fluid escapes. In some old standing cases, owing to defective circulation, a true œdema may be superimposed, and in these cases a correct diagnosis is often attended

by very gratifying results.

Under the influence of thyroid, this mucoid thickening is one of the first signs to show amendment. Not that it is really the first thing to give way; an irritating cough, a severe pain in the back, or an intolerable headache may go, but these are only subjective symptoms. The myxœdematous swelling is a sign. We see it disappearing with our own eyes, and the patient's friends notice it too. How we all run after signs! In our intense desire to see and touch, we place upon a pedestal a sign of little or no importance, and apotheosize it, while we pass by, almost without a record, a symptom that may be colouring the whole tenor of a life; because, forsooth, we cannot put a mere symptom under a microscope, or preserve it in spirits and place it in a museum to demonstrate it. Here we have a disease even named after a sign—a sign too, that appears in the later stages, and when fully developed, is associated with such a congeries of symptoms, that one could then well describe the condition or the patient, in the words of the cynical Jacques, as "Second childishness and mere oblivion."

Now, although we find that this myxœdematous swelling is one of the most characteristic of all the symptoms, it is one of the later developments, and it is important to diagnose the condition at a much earlier date. Even in the skin, we see earlier changes. If the facies of various cases is examined, we shall find in all, with the exception of those that have gone on to almost complete athyroidism, that the face is somewhat flushed, this flush being most apparent over the malar bones, which are rendered conspicuous by the presence of blue-red, deeply injected vessels.

In those cases, which have been a sequela to exophthalmic goitre, this facies is associated with the prominent eye, a vestigial remnant of that disease. At one time, I was of opinion that the flushed face and injected vessels were vestigial remains of a goitre as well. But further experience has shown that it is present in cases of insufficiency, in which one can find no evidence of a pre-existing goitre. One might suggest that the hyperplasia of the thyroid, from which such a case must have suffered as a forerunner of the subsequent atrophy, was attended by a hyperthyroidism sufficiently

moderate to pass unnoticed by the patient. That certainly is possible, but my experience of hyperplasias of the thyroid, resulting from the toxæmias of disease, is, that in most cases they pass from hyperplasia to atrophy without symptoms, until the advent of thyroid scarcity.

This peculiar facies, when it is complicated with the prominent eye, is often a stumbling block to diagnosis. I reproduce two photographs (Figs. 3 and 4, Plate XXXVI., page 327). Twelve years ago this patient suffered from exophthalmic goitre. The first photograph was taken in the eighth year of her illness, when the myxœdematous condition had arrived. The heavy featureless face with its vacant expression will be noticed. The second photograph is one of the same lady after being cured of her myxœdema. On looking at the second photograph, the opinion would probably be hazarded that the woman was suffering from exophthalmic goitre; yet as a matter of fact, she has thyroid insufficiency, and is only kept in health by the constant administration of thyroid tabloids. In these cases, in which the facies of thyroid insufficiency is complicated by the prominent eye, the clinical history of the patient is absolutely essential to a correct diagnosis.

The appendages of the skin also suffer. The nails frequently become brittle, and their growth is slow. The sweat glands and the sebaceous follicles suffer atrophy, and the skin becomes dry. The condition of the hair, however, is more important for diagnosis. It gets thin, dry, and brittle. It looses its lustre, and the skin of the scalp can be seen dry and dull through the attenuated hair. Under the influence of thyroid gland substance, the hair recovers its gloss and fullness.

In the earlier part of this article, I called attention to the slight enlargement of the thyroid gland which takes place in the early months of pregnancy. Recently, apart from any suggestion of mine, a young married woman, in the fifth month of her pregnancy, said to me, "My hair has got much fuller and thicker of late." There are other cutaneous irregularities that arise in the course of this disease; these, however, are incidental and peculiar to the individual, and are not typical.

One case of psoriasis, however, is so illustrative of the direct connection existing between healthy ovarian and thyroid activity, that I mention it. The patient was a young mother, suckling her fifth child. She came to consult me about the child, but her own hands and arms were so covered with a scaly psoriasis, that I could not help examining the condition and inquiring about it. She told me that her whole body, with the exception of her face and neck, was similarly affected. The patches varied from the size of a threepenny-bit to that of a shilling, and the surrounding skin had that peculiar bronzed appearance which comes to the skin of a brunette who has been much exposed to the sun. She said this condition had arisen after every confinement, and persisted in spite of treatment till the termination of suckling and the re-establishment of her monthly period. She never now tried anything for it.

Dr. Byrom Bramwell, who was the first to call attention to the cutaneous eruptions of thyroid insufficiency, had not then published his paper, and the theory of interaction among the various internal secretions had not been formulated. I did not, therefore, suspect the real *causa morbi;* but, in view of modern research, I now look back upon that case with regret as a missed opportunity.

Cases of psoriasis are so commonly met with in general practice, that one has frequent opportunity of trying freshly vaunted methods of treatment. As far, however, as psoriasis is concerned, I have to record that, in my experience, thyroid therapy has met with a succession of failures. I am now quite of opinion that, however beneficial it may be in some cases, these cases are the very few. The great majority are not influenced by thyroid administration at all, and, on this account, I reason, they are not due to thyroid insufficiency, but to some other cause yet to be discovered.

Another very important symptom, seen in the early stages, is loss of vigour. The bodily energy seems to disappear, and work which aforetime was easy and pleasant becomes a burden. The deprivation from the system of a sufficiency of the thyroid secretion depreciates metabolic changes in every department of the body. Every process slows down. The sweat glands function slowly, the skin desquamates slowly,

the nails grow slowly, the patient speaks slowly, thinks slowly, acts slowly. The temperature of the body is lowered to subnormal, and vital processes are everywhere depressed. This loss of energy is an early symptom, and as the scarcity passes to complete starvation of this life-giving and energizing secretion from the system, the tiredness and lethargy increase concurrently, until complete invalidism is reached.

All sorts of irregular symptoms may be added to these salient conditions. For instance, a male patient had a most distressing cough, which quite disappeared during treatment. The patient, whose photograph is reproduced (Fig. 5), developed delusional insanity. Some patients suffered from headaches and sleeplessness, while others had severe backache. One patient, who experiments a little with herself, states that if she misses taking the tabloids for a time, the sleeplessness returns, and she develops such pain across the loins that she can with difficulty walk 50 yards.

Symptoms of this sort are purely incidental to the real disease, and one cannot found a diagnosis upon them. But they are often very distressing, and the fact, that they clear up under the influence of treatment, establishes their dependence upon and association with the thyroid scarcity.

This power to produce comfortable sleep in some of these cases is one of the remarkable properties of thyroid substance. It is only two weeks since an elderly lady said to me, "Be sure and let me have some more of the little brown tabloids. Since taking them I have enjoyed good sleep, and I had almost forgotten what it was like." Other patients tell a like story.

I have not dealt with thyroid insufficiency of childhood at all. Children form a large class by themselves, and the conditions found in them, occurring as they do in the developmental period of life, are quite different, for the most part, from the manifestations of this disease among adults.

In conclusion, I should like to answer very briefly, out of my own clinical experience, Dr. Geo. Murray's query, whether these patients are ever again able to do without the adventitious aid of thyroid substance.

In the case of Mrs. M., two years have elapsed without any treatment, and, according to her report, "she is as well

Plate XXXVII.

Fig. 3.—*Photo of Mr. S., aged 45 years. He states, "Two years ago I complained of over-sleepiness. I could only walk about 50 yards when my back would give me some trouble. My breath was also affected. My breasts were hanging from two to three inches. My hands were so swollen I could not close them. My boots would not fit me and I had to get a special pair made two sizes larger. I measured 47 inches round the waist and wore an 18 inch collar. My waist measurement is now 38 inches and I now wear a 15½ collar. The pain in my back has gone and I can now do my work with ease and comfort. Previously I suffered from a constant cough which quite disappeared during treatment. When I began treatment on December 2, 1912, my weight was 14 st. 2 lbs. Today it is 11 st. 5½ lbs."*

Fig. 6.—*Mrs. J., aged 63 years, with history of 20 years' illness and invalidism. Typical case of myxœdema. She is now able to do her housework. Sleeplessness and fear of falling asleep were two of her most painful subjective symptoms. These rapidly disappeared with the taking of thyroid. Note the carrier-pigeon eyes.*

Fig. 7.—*Mrs. M., aged 60 years. History of 20 years' invalidism. Mrs. M is able to keep herself in good health by using 18 tabloids (5 gr.) in the 3 months. She is a true thyroid-insufficient. A case that can be kept in health by using 2½ grs. of thyroid extract 3 times weekly cannot be suffering from complete atrophy of the thyroid gland. Such cases have their analogue in those moderate diabetes where, after treatment, a slight degree of carbohydrate tolerance is found to exist*

as ever she was in her life." Her own thyroid has evidently taken up the parable again, and is functioning normally and sufficiently for her requirements. She, however, is a comparatively young woman, and her cure took place before she had reached the degenerative period of life.

Then the cretinoid child, when cured, remained cured. Indeed, I do not know one single child, that I have treated to the passing of his thyroid insufficiency, who has not subsequently remained well without further aid. But other patients are kept in health only by continual thyroid feeding; these, however, are all in the degenerative period of life, and that is my experience in regard to all my other cases who developed this disease in the decadent period.

If the patient is a child, the thyroid will almost certainly again functionate sufficiently for healthy metabolism. If the patient is between 20 and 30 years of age, there is still some hope of that desirable condition being attained. But if the patient has passed the 40th year, the thyroid gland rarely, if ever—never, in my experience—is able again to deal with the thyroid needs of the system.

Practical Notes on the Internal Secretions.

ADRENALIN-PITUITRIN TREATMENT.

Rohmer points out that disadvantages have been found to attach to the use of adrenalin by itself, both by intravenous and by hypodermic injection. In the former the rise of blood-pressure is only of short duration, and is followed by a fall, which may be fatal, to below the original figure. In hypodermic administration, the effects are much different, because only a small proportion of the drug reaches the circulation, and then only after a delay of several hours, in consequence of the strong local vaso-constriction set up, whereby 94 per cent. of the substance is used up. It is for this reason that large doses may be repeated frequently without harm.

Kepinow proved, experimentally, that the action of adrenalin is favourably influenced if the intravenous injection of the drug is preceded or combined with an injection of pituitary extract. Matthes tried this combination in clinical work with very good results, and Rohmer during the past few months has been using it on children of all ages. He has found it of great service in the severe circulatory troubles due to pneumonia, diphtheria, and typhoid fever. To young children, he gave 0.25 cc. of the 1 per mil. pituitary preparation and 0.5 cc. of the 1 per mil. adrenalin solution. Double doses may safely be given to older children. He found all the commercial preparations were equally effective. The dose of the combined drugs was usually given every six hours, and in the interval an injection of camphor or caffeine. In one grave case of diphtheria, the treatment was continued for 12 days with one intermission. This produced a very critical condition, which was relieved by renewing the injections. In a case of pneumonia, in a girl 18 months old, severe collapse set in, the blood-pressure falling to 60 and the pulse running up to 200. Two minutes after the injection the blood-pressure rose to 80, and to 90 in another two minutes. After a quarter of an hour, it sank to 85, and then to 80, at which it remained for five hours. Another injection was then given, and the pressure remained at this figure with continued improvement in the general condition. Careful observations of the pulse and blood-pressure in this case showed that the effect of the combined injection was maintained for about six or seven hours.—(*München. medizin. Wochenschr.* 24, 1914.)

TREATMENT OF OSTEO-MALACIA WITH ADRENALIN.

Dupasquier reported recently, in the *Lyon Médical*, the case of a woman of 50 years of age, in whom osteo-malacia set in with intense generalized pains in all the limbs. The cause of the attack could not be traced; the patient had no symptom of tuberculosis past or present, she denied having had syphilis and a Wassermann test proved negative, and she had never been pregnant. The bones affected were the right humerus, the tibias,

the ribs, and the sternum, all of which became much softened and showed considerable loss of substance in the bone, when examined by radioscopy. She was treated on Bossi's lines, by injections of from ½ to 1 cc. of 1 per mil. solution of adrenalin every two days. After the fifth injection the patient felt much better, the pains were very much less, movements were made more easily, and the bones were not tender on palpation. She began to eat well and put on flesh. She received 17 injections, and the improvement persisted. The softening of the bones does not appear to have been influenced, but all pain and tenderness disappeared, so that the patient was able to get about easily and in comfort.—(*Journ. des Praticiens.* No. 26, 1914.)

ADRENALIN AND PITUITARY EXTRACT IN OPHTHALMIC WORK.

Arganaraz reports excellent results from the use of a combination of adrenalin and pituitary extract as a vaso constrictor and hæmostatic in ophthalmic surgery, and as a therapeutic agent in conjunctival affections. The solution used was composed of 20 cc. of a solution of fresh extract from the posterior lobe of the pituitary body of the ox, containing 0·2 g. per cc., with 1 cc. of the 1 per mil. solution of adrenalin. No effect was produced upon the corneal epithelium by frequent instillations of this solution, and the ischæmia of the conjunctiva produced was not obtained so quickly as when adrenalin is used alone, but the effect lasted longer and appeared to extend more deeply into the tissues. The pupil dilates slowly, but no effect was produced upon accommodation or upon the tension. Arganaraz considers that this combination is very useful in operative work, such as sclerotomy, iridectomy, tenotomy, and operations for pterygium, chalazion, and the like. When combined with pilocarpine, eserine, or atropine, the action of these drugs is increased.—(*Rev. de Thérapeutique méd.-chir.*, December 1913.)

THYMUS EXTRACT IN GRAVES'S DISEASE.

R. Hirsch was led to try thymus extract in this disease by the fact that children can stand thyroid medication much better than adults, and very seldom suffer from Graves's disease. In them the thymus gland is still active, and is able to counteract the effects of any hyper-secretion from the thyroid gland. Tablets of thymin, containing 0·5 g., were given twice a day, and in one typical case an increase of 30 lbs. in weight was obtained in two months, with marked general improvement which rendered a proposed operation unnecessary. Several patients, who had been operated upon without benefit, were greatly improved by this treatment, losing all their symptoms.—(*Deutsche medizin. Wochenschr.* 44, 1913.)

PITUITARY EXTRACT IN GRAVES'S DISEASE.

Pal reports the case of a man, of 32 years, whose symptoms included a pulsating goitre, von Graefe's sign, marked tachycardia, tremor of hands and feet, dyspnœa, and loss of weight (30 kilos. in 12 months). He was given hypodermic injections of pituitary extract—·04 g (gr. ⅔) in each. The treatment was continued for three months, 70 injections in all being given. He improved considerably, the pulse dropping from 140 to 100

and under, the tremor and insomnia being very much less, the breathing easier, and the weight increasing from 46 to 53 kilos.—(*Semaine médicale*, January 1914.)

PITUITARY EXTRACT IN OBSTETRICS.

Watson is of opinion that the chief field of usefulness of pituitrin is in the first and second stages of labour, when there is delay due to the feebleness of the pains, alone or when combined with other complications, such as malpositions of the head, malpresentations, multiple pregnancy, slight narrowing of the pelvis, etc. It gives good results in many cases of post-partum hæmorrhage, but is not superior to the various preparations of ergot. It has the power, however, of sensitizing the uterus, so as to allow these preparations to act more powerfully, the combination being most effective.—(*Monthly Cyclopedia and Medical Bulletin*, August 1914.)

LEUCOCYTE EXTRACTS IN INFECTIVE PROCESSES.

Hiss and Dwyer have treated over 300 patients suffering from various infections with this extract, and report the results obtained in erysipelas. The cases were of all types and grades of severity, most of them being of the severe type in which other remedies had been tried, the infection was well established, and the general symptoms marked. In every case there was a marked reaction, usually shown by a fall in temperature and a rapid improvement in the general condition. In nearly every case, the symptoms disappeared within a few hours after the first injection. Headache, nausea, and vomiting disappeared, and the mind became clear and quiet. In cases treated within 48 hours of the onset, the disease practically ended by crisis. In cases treated later in the course of the disease, the effect on the temperature was not so marked, but the general improvement in condition was obtained and the disease was cut short.

Locally, the burning and aching pain disappeared in a few hours, and the rash soon faded away.

The average duration of treatment in this series was just over three days.—(*Monthly Cyclopedia and Medical Bulletin*, October 1914.)

TREATMENT WITH CORPUS LUTEUM.

Dannreuther considers that corpus luteum, fresh or the dried extract, is very much more effective in action than ovarian preparations. He has obtained good results from giving it in the following conditions:—Functional amenorrhœa, scanty menstruation, dysmenorrhœa of ovarian origin, reflex nervous troubles of the natural and the artificial menopause, neurasthenia, sterility if not due to infection or mechanical obstruction, impaired function in one ovary, frequent abortions not due to disease or displacement, and excessive vomiting in pregnancy.

He found that the treatment produced some giddiness at first, but this soon passed off and tolerance was established. The pulse rate is usually increased, but there is no rise of blood pressure. The extract used should be obtained from the ovaries of pregnant animals only. During the treatment it is necessary to keep a constant watch on the blood-pressure of the patient.

Dannreuther used an extract obtained from pregnant cows, which represents about six times the weight of the fresh moist substance. He did not give any fresh substance nor the ordinary desiccated extracts. The usual dose given was one of five grains in a capsule three times a day. This quantity was very seldom increased, but occasionally ten-grain doses were foundnecessary. After taking five-grain doses of the extract for a week, a fall in the blood-pressure is usually found to have occurred, and if this has taken place too quickly, the administration must be suspended for a time. The height of the blood-pressure must be noted carefully before beginning the treatment, and during its course readings must be taken every week. If the fall is as much as 15 m.m., the treatment must be stopped until at least 10 m.m. of this fall have been regained. The resumption must be made carefully. The blood-pressure should never be allowed to fall below 90 m.m. in any case.

Dannreuther considers it important always to make use of freshly prepared extract, and puts a limit of three months after manufacture to ensure reliability. He has treated about 80 cases, and obtained good results with few exceptions.— *Journal of the American Medical Association*, January, 1914.)

OPOTHERAPY IN CHRONIC OSTEOARTHRITIS.

P. W. Roberts treats this disease by giving glandular preparations, rest, diet limiting the in-take of calcium, and high frequency current (d'Arsonval). The glandular preparations are from the thymus, thyroid, and pituitary, all of which have a direct influence upon nutrition, although no single one of them is able by itself to regulate metabolism. The thyroid is the least used in this disease, for it is rarely useful alone, but may be so, in combination with the other glands, when the weight has increased. In that case, as soon as the full physiological effect has been obtained, the dose must be made much less, and kept reduced during treatment. The thymus is slow in producing effects, but these have been proved to be of value in osteoarthritis, whether of Nathan's metabolic type or in the chronic infective form. It is given in doses of 10 or 15 grains, three times a day, for some months (six at least). It should not be given when there has been a rapid increase in weight because it often stimulates general nutrition very notably. Fresh preparations must be used, because it loses its activity very quickly. The pituitary gland, given by intra-muscular injections of 1 and 2 per cent. solutions of the whole body, has yielded good results. 1 c.c. of the 1 per cent. solution is injected daily for a fortnight, and then the 2 per cent. solution is used. The blood-pressure must be taken occasionally and the urine must be tested for sugar. Tablets of the whole gland are not to be relied on, but will sometimes produce the same effects as the injections. The posterior lobe alone does not appear to have any definite effect upon joints, but Roberts has had good results from giving capsules of the powdered anterior lobe. This combined with thymus seems to be more effective than thymus alone, and is given in doses of two grains in capsules, three times a day.— (*Medical Record*, May, 1914.)

PITUITARY EXTRACT IN HÆMOPTYSIS.

Houssay has advised, since 1911, the use of pituitary extracts to stop hæmoptysis, but these have only been tried of late years in hæmorrhage

from the lungs. Their effectivity depends upon three factors, which act together. 1. *Pulmonary hypotension*, due to their initial depressant effect upon the heart's cavities, and, consequently, upon the right heart. These facts were proved by Houssay in the horse by means of Chauveau and Marey's sounds. 2. *Pulmonary vaso-constriction*, demonstrated by Dale. 3. *Acceleration of the coagulation of the blood*, determined by Weill and Boyé, and others. This factor is the least important.

The hæmostatic action of these extracts has been proved by Wiggers, Rist, Leon Bernard, and Flandrin. Several patients have been treated by Destéfano and Coin. The latter has had four cases of hæmoptysis, in which the bleeding was stopped very shortly after the injection. The extract is well tolerated by patients: the only fatal case after its use was reported by Jacquerod. The injection was followed by an asystolic crisis with dilatation of the right heart, and the autopsy showed the intra-ventricular rupture of an arteriole, to which possibly the drug had contributed to a small extent. The substance to be used should be an extract, pituitrin or any other, standardized to 20 per cent. of the posterior lobule of the pituitary body. Not more than one-half of a c.c. should be injected into a vein in the bend of the elbow, intra-venous injection being the preferable method of administration. The injection is followed by pallor, malaise, feeling of oppression in the epigastrium with a tendency to lipothymia. These symptoms clear off quickly, except the pallor. After the hæmorrhage is stopped, the sputa remain stained for some time. When the sputa are only slightly tinged, and the bleeding is not free, the pituitary extracts are not of much service and should not be used.—(*Revue de Thérapeutique med.-chir.*, July 15, 1914.)

TREATMENT OF DIABETES INSIPIDUS WITH PITUITARY EXTRACT.

Biach reports the case of a man, 21 years old, who had suffered since the age of 7 seven years from intense thirst and headache. He passed from 12 to 15 litres of urine (sp. g. 1003–1005) daily, and drank 20 litres of liquids. Injections of pituitary extract, 0·10 g. three times a day, brought about a decrease in the polyuria to 9½ litres. Larger doses brought this amount down to 4 litres in the 24 hours, increased the specific gravity of the urine, and lessened the thirst. In another case the polyuria was reduced from 7 litres to 2½.

The treatment is specific, for, in a healthy man, no decrease is caused in the secretion. It appears to act upon the nervous centres and does not affect the renal function directly, but lessens the abundant micturition by moderating the thirst. Its effect is not persistent, for it has passed off the day after the injection. The infundibular pituitary extract must always be used, and the administration must be by hypodermic injection, for even in large doses it is quite ineffective when given by the mouth. —(*Rev. de Thérap. med.-chir.*, March 1, 1914.)

ADRENALIN IN PERSISTENT VOMITING OF PREGNANCY.

Pedro Valle adopts the toxic theory of the cause of vomiting in pregnancy. That condition induces increased function in the suprarenal bodies, which contributes towards the defence of the organism. When

this hyperfunction of the adrenals is not produced, vomiting sets in. It is, therefore, logical, in these cases, to make up for this deficiency of the endocrinous glands by the use of adrenalin. It is not injurious to either mother or child, is easily given, acts quickly, and stops the vomiting.—(*Revue de Thérapeutique med.-chir.*, January 1, 1914.)

TREATMENT OF GRAVES'S DISEASE BY INJECTIONS OF PITUITARY EXTRACT.

Pal treated a man, 32 years of age, suffering from exophthalmic goitre —trembling, insomnia, diarrhœa, tachycardia, &c.—with pituitary extract. The patient was in bad general condition and had lost 30 kilog. in weight in 12 months. He was ordered vegetarian diet, and given hypodermic injections of pituitary extract. In three months he received 66 injections, each of 4 centigr. of the extract. His weight increased 7 kilog.; the pulse-rate fell from 140 to 92; there was less shivering; and sleep became quieter with easy respiration.—(*Revue de Thérapeutique med.-chir.*, March 1, 1914.)

ADRENALIN IN RHEUMATISM.

Jaistöck has had excellent results in rheumatic affections from the use of subcutaneous injections of 1-in-1,000 solution of adrenalin. He gave from 0·5 to 1 cc., at most 2 cc., *per diem*. In most cases the pain and swelling dispersed in an hour or two, but returned some hours later. The duration of the disease was cut short appreciably. The after-effects of the injections were more or less severe shaking of the hands, sometimes of the whole body, without any feeling of cold. Usually there was a feeling of warmth, with sweating. Inflammatory affections of the nerves seem to be favourably affected by adrenalin. Two cases of sciatica were much improved after a few injections.—(*Med. Klinik.* No. 11, 1913.)

ADRENALIN IN WHOOPING-COUGH.

Fravost describes the treatment adopted by Chevrel, in the Hôtel-Dieu at Rennes, which chiefly consists in the use of adrenalin. As a general rule, inhalations are employed as well, composed of 2 parts of salicylate of methyl and 1 part of eucalyptol. About a teaspoonful of this mixture is placed in a saucer, close to each patient, and allowed to evaporate into the room. The quantity is replenished three times a day to ensure continuous medication. This method, which is easy and not expensive, is considered by Chevrel to be of very great service.

The average dose of adrenalin given is one drop of the 1-in-1,000 solution each day for every year of age. This dose may be doubled without inconvenience. In the majority of cases an excellent effect is produced, especially on the vomiting, which gets less almost at once. The effect on the paroxysm is not so marked. The general condition is greatly improved by the adrenalin, for the cessation of the vomiting allows nutrition to be carried on properly. Those patients who have been treated with adrenalin have been noticed to be free from complications and relapses.—(*Journ. de Med. et de Chir. prat.*, June 10, 1914.)

TREATMENT OF HYPERACTIVE INTERNAL SECRETING GLANDS WITH X-RAYS.

Zimmern and Cottentot claim that, without going so far as suppression of secreting function, irradiation suitably regulated can lessen the functional

activity of a gland. All the glands of internal secretion are susceptible to this treatment; their resistance to the action of the rays is always greater than that of the glands of external secretion.

OVARIES.

It has been proved that by treating uterine fibromata by ray treatment, an artificial menopause is induced with its usual concomitants.

THYROID.

To reduce the functional activity of this gland, strong doses of X-rays are necessary. The results of this treatment on exophthalmic goitre are extremely variable, but the same thing applies to all other methods of treatment of this disease. It is suggested that what is in question is the matter of doses.

PITUITARY GLAND.

Two observations have been recorded, one of which, reported by Beclère, seems conclusive. It may, therefore, be hoped that the development of gigantism and of acromegaly may be checked by reducing the functional superactivity of the pituitary gland by means of irradiation, especially when these are observed in an early stage.

THYMUS.

Eight cases have been reported and the results prove that in a few days irradiation will effect the disappearance of the stertor, the suffocating attack, and cyanosis, characteristic of hypertrophy of the thymus gland in children.

SUPRARENAL BODIES.

These are known, nowadays, to play an important part in the pathogenesis of atheroma and of arterial hypertension. Zimmern and Cottentot have treated 27 patients showing permanent arterial hypertension. Only 4 of these failed to show any modification of pressure, whilst in the others a fall of from 1 to 7 cm. Hg. was obtained which lasted in some cases for 7 months. With others it was necessary to repeat the irradiation from time to time. The greatest successes were obtained in the pure hypertension cases, 15; in these, besides the high pressure, all the functional symptoms were very greatly influenced. In 7 atheromatous cases, the results were not so striking. Albuminuria, if present, was not affected at all; it is a contra-indication for the treatment in diabetes, if the amount of sugar increases, whilst the blood-pressure is lowered.—(*La Presse médicale*, February 18, 1914.)

THE PRACTITIONER.

MARCH, 1915.

THE INJECTION TREATMENT OF HÆMORRHOIDS.

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(*a*) By F. SWINFORD EDWARDS, F.R.C.S.

President of the Sub-Section of Proctology, Royal Society of Medicine; Consulting Surgeon to St. Mark's Hospital for Diseases of the Rectum, etc.

THIS is a subject to which I devoted some time and attention, when I was an Assistant Surgeon to St. Mark's Hospital. In 1888, a paper of mine, dealing with the subject, was published in the *British Medical Journal*, and gave the results of many cases treated in the Out-patient Department. Mr. Ivor Back's paper on hæmorrhoids in the October, 1914, number of THE PRACTITIONER and Sir James Goodhart's comments thereon in the December, 1914, number, have re-awakened my interest.

Let me say at once, that I have never repented having recommended this procedure to the profession, now 25 years ago. The favourable opinion I then formed of it, from an experience of over 100 cases, has, with time, rather increased than diminished.

We all see many cases of internal hæmorrhoids which require *no* operation, but can be dealt with successfully by ointments, suppositories, attention to diet, and the careful regulation of the bowels, etc.; but when hæmorrhage is a marked feature, when protrusion takes place at stool or on

exercise and necessitates replacement by the patient or an attendant, or when various reflexes are induced undermining the patient's health, some form of operation is necessary.

After an experience of some 6,000 operations for piles, I am strongly of opinion that what is known as *Salmon's operation* is the best in the majority of cases. Whitehead's, which bid fair at one time to take its place, is, I am glad to say, rapidly falling into disfavour, for I have seen many ill-results following this operation, even when carried out by skilled hands. The *clamp and cautery* operation in uncomplicated cases of internal hæmorrhoids, when the piles are not more than three in number, is quite excellent. Convalescence is rapid, pain negligible, and hæmorrhage no longer to be feared if only a small rubber flatus tube is inserted and left in for three or four days.

With regard to the *Injection Treatment* of hæmorrhoids, the cases suitable are those of *reducible* internal hæmorrhoids, which are uncomplicated by external tags or piles—fissure or fistula; cases in which the patient cannot afford to lie up, which is usually the case with medical practitioners; and those in which an operation under anæsthesia is either objected to by the patient or, on account of heart or lung trouble, is considered risky. My method of procedure is as follows :—

After a warm boracic enema, the piles are extruded at stool. The patient is then placed on a couch in the knee-elbow position, and the piles mopped over with a little warm lysol or other antiseptic lotion. A hypodermic syringe is filled with the following solution :—

℞	Acid. Carbol. - - - -	gr. xxiv.
	Glycerini - - - -	ʒ i.
	Aquam ad - - - -	ʒ ii.

At first, I used a 10 per cent. solution, *i.e.*, half this strength, but I have found the stronger much more efficacious.

The needle, of good lumen, is then passed into the centre of each prolapsed hæmorrhoid in turn, from 3 to 6 drops being injected according to the size of the pile. This is usually quite painless. Swelling occurs at once, so the sooner the piles are returned the better. The patient is then

allowed to go home, with a caution to return the piles at once should any prolapse occur, otherwise strangulation and sloughing might ensue. A second injection is sometimes necessary after the lapse of a month or two, but in many cases recurrence, if it takes place at all, is postponed for a year.

When circumstances permit, I prefer to carry out this treatment in a patient's own bed-room, in order that he may rest quietly in bed until the next day. Should the piles prolapse after an action and not return of themselves, the patient is instructed how to replace them with as little delay as possible.

I am thoroughly in accord with the general purport of Mr. Back's paper, though I differ from him in the technique as well as in the solution used in the injection treatment. If there is no risk in injecting all the piles at one sitting, surely this must be the better plan !

This treatment is absolutely contraindicated in cases of irreducible, inflamed, or sloughing hæmorrhoids. I quite agree with Sir James Goodhart, that the treatment of hæmorrhoids by injection might be employed more frequently than it is, but my experience differs from his in the after-result of the ligature operation (Salmon's), when it has been carried out by those who have had some experience of it; in competent hands, it is free from all risk. The stay in hospital or a nursing home averages two and a half weeks. It is a radical cure, and should give rise to no local trouble afterwards; indeed, in my experience, local troubles including constipation, various neuroses, and the "mens conscia recti" become things of the past.

The reason why I do not recommend the injection treatment in *preference* to an operation is, that patients who come to us have usually suffered for some considerable time, and want a cure, not treatment with a possibility or even a probability of a cure.

To show how comparatively few cases are fitted for the injection treatment, I may instance to-day's afternoon work at St. Mark's Hospital. I had eleven cases of internal hæmorrhoids to operate upon, but in only one there was no complication; amongst the others were four cases of fissure, one of anal ulcer, one of thrombosed internal pile, and in four

there were also external piles.

In conclusion, the great advantage the injection method has over all others is, that it does not lay the patient up. No anæsthesia is required, and therefore no post-operative sickness to be dreaded. It is practically painless, is devoid of risk, if only the usual antiseptic precautions are taken and due obedience given to instructions. The patient begins to get better at once; hæmorrhage and prolapse cease or diminish rapidly. If one injection does not suffice, one or two more can always be given.

(*b*) By P. LOCKHART-MUMMERY, F.R.C.S.

Senior Surgeon, St. Mark's Hospital and Queen's Hospital for Children: Honorary Surgeon, King Edward VII.'s Hospital for Officers.

In his article, published in the December, 1914, number of THE PRACTITIONER, criticizing Mr. Ivor Back's paper, Sir James Goodhart raised the question of the best treatment of internal hæmorrhoids, and, personally, I was much interested in reading his views on this subject. The consulting physician naturally sees the results of operative procedures from a different point of view to that of the surgeon, and there is nothing so interesting as studying a subject from a point of view other than one's own.

I notice that Sir James seems to have a preference for the treatment of internal hæmorrhoids by injection, and that he has asked for the opinion of others on this question. The treatment of internal piles by injection is, in my opinion, excellent in suitable cases, and is a method of treatment which I have used extensively since I first learnt it when I went to St. Mark's Hospital. Hardly a week passes in which I do not treat some patient by this method, and I have been much pleased with the results in selected cases. It is, however, in my opinion, not a suitable method except in selected cases, and recurrence is certainly not uncommon, although one can always repeat the injection at a later time.

This treatment for internal piles was, I believe, first brought to the notice of the medical profession in this country by my colleague, Mr. Swinford Edwards, in an article in the *British*

Medical Journal, October 13th, 1888, and he was, I think, somewhat criticized for recommending what was considered a quack remedy. Ever since that time, however, this treatment has been in use at St. Mark's Hospital, and with good results. Recurrence of the hæmorrhoids certainly takes place not infrequently, and a certain number of patients have to be operated upon subsequently. There have been cases of severe pain and strangulation as the result of injection in unsuitable cases, when there was a large mass of prolapsing piles, or when the patient was not careful to prevent the piles from prolapsing after the injection.

Sir James asks whether any cases of embolism have occurred after the injection treatment. Personally, I have never seen or heard of a case of embolism occurring after injection, during the whole time I have been practising at St. Mark's, and the only case I have met with, in which a serious result followed this treatment, was one in which I inadvertently injected a patient who was the subject of hæmophilia. He very nearly died of hæmorrhage from the needle puncture. Fortunately, we were able to save his life, but, needless to say, the injections were not continued.

While I agree with Sir James that the injection treatment is satisfactory in selected cases, I cannot agree with his conclusions as regards operation. It is not always fair to draw conclusions as to the merit of any particular operation, without taking into consideration the surgeons who perform that operation. Piles are extremely common, and to say that the operation is one of the most frequently performed of all surgical procedures is probably not overstating the case. Further, every medical man thinks he can operate for piles, and as a result of this, there is probably no other operation which is so frequently performed by unskilled operators. Many surgeons, too, look upon the operation for piles as one which requires no particular care and very little, if any, after-treatment. There are still a good many surgeons who operate for piles without even attempting to asepticize the tissues beforehand, and who see with equanimity fæcal material soiling the wounds during the operation. Under these circumstances, it is hardly surprising that there are a considerable number of patients who have been disappointed at the result of an operation upon

their piles.

The real truth is, that an operation for piles requires to be performed with considerable care and not a little skill, and, perhaps more important than all, requires very careful after-treatment; if the operation is performed under these conditions, there is, I believe, no surgical operation which can show more uniformly excellent results. At the present time, a properly performed operation for piles should not be followed by any pain requiring the use of morphia, and the patient should be cured of his trouble without its being possible to detect a month or so later, on close examination, that an operation has been performed.

It is only at a hospital like St. Mark's that one has the opportunity of observing the results of this operation, performed under more or less uniform conditions. At that institution a careful record of cases has been kept for many years, and some three hundred operations for this condition alone are performed in the course of a single year. The average patient leaves the hospital cured in less than 14 days from the time of operation, and the records show that the proportion who require any further treatment is exceedingly small. I attempted some years ago to work out the percentage of recurrences after the ligature operation from the hospital records, and it came to considerably less than 1 per 1,000.

To sum up, I agree with Sir James Goodhart in considering that the injection treatment is harmless, and in selected cases gives very good results; but I agree with Mr. Ivor Back in considering it inferior to operation, when this can be carried out by a skilled surgeon under suitable conditions.

(c) By JAMES EADIE, F.R.C.S.

DURING the last ten years, I have made, in hospital and private practice, about 2,000 injections for hæmorrhoids, adopting the technique advocated by Mr. Dudley d'A. Wright, which is substantially that described by Mr. Ivor Back in THE PRACTITIONER, October, 1914.

It is to my mind the treatment of choice for primary hæmorrhoids, and that to which I would prefer to submit myself,

were I in *loco patientis*, in the belief that it conforms to the standard "cito, tuto, et jucunde." I always advocate it in preference to operation, except in those cases when for some reason or another the patient has to submit to a general anæsthetic; in that case, it is well to take advantage of the anæsthesia, and operate on the piles at the same time.

In those who submit to a complete course of injections, I believe the percentage of cures is as high as by any method of operation, and recurrence is in my experience the exception. Many patients are so greatly benefited by a few injections, that they cease attending with the cessation of their symptoms, although piles are still demonstrable by means of the proctoscope. It is not to be wondered at, if in course of time these give the patient discomfort, but even in that case the injections appear to act for a time after their discontinuance, and a return of symptoms does not occur in anything like the percentage of patients one is prepared for. When in the course of years the symptoms do recur, the patient turns up for a few more injections, is made comfortable, and goes his way, until, if ever, the piles again make their presence felt.

Unlike Mr. Ivor Back, I inject three or four piles at each séance. That may account for the treatment being more prolonged in his cases.

I have not experienced any dangerous complication resulting from the treatment, and have never met with embolism.

The mishaps I have observed are mainly two:

(1) Pain—which results if the injection is made too near the muco-cutaneous junction, or if the pile is allowed to prolapse and remain prolapsed after it is injected. I always warn patients that their part in the treatment is to return the piles immediately they prolapse, during the 24 hours subsequent to injection; if they fail to do so, they will experience pain, which is no part of the treatment.

(2) Sloughing of the mucous membrane over a small area producing ulcer or fissure. This, I imagine, results from injecting too closely under the surface of the mucous membrane. I endeavour to inject at least a quarter of an inch deep, and as near where the veins leave the pile—*i.e.*, as high up the anal canal—as possible.

When first, at the instance and on behalf of Mr. Dudley

d'A. Wright, I undertook this method of treating hæmorrhoids, I was imbued with the scepticism of the surgical text-books; the experience I have had makes me enthusiastic in its favour, and I fail to see why this method does not find more favour with the profession.

(*d*) By ROLLIN H. BARNES, M.D.

Editor of "The Proctologist," St. Louis, U.S.A.

ALTHOUGH not out of my own experience, I cannot help saying something in reply to the article written by Sir James F. Goodhart, in the December, 1914, number of THE PRACTITIONER. His position is that of many a one who has looked upon the operations of the ligature, clamp, cautery, and Whitehead as the ideals for hæmorrhoids. They were yesterday. Surgery has advanced, and I do not believe that they are up to the standard of modern surgery. But because this is so, why take a step backwards to the injection method? This method will not meet the demands of exactness in modern surgery.

It seems peculiar that a surgeon to-day will do one thing in one part of the body, and forget all about it when he comes to another part of the body, which he considers with (I might say) superstition. No modern surgeon would think of cauterizing a tumour on the skin surface, especially if it is not infected. It makes one laugh to see a modern surgeon, when it comes to a pile, put a ligature round it, cut it off, and leave a stump that will for ever bother his patient. We might say the same for the clamp and cautery. What should we think of a modern surgeon, who did a similar thing on the skin surface, and expected a slough in three to eight days?

Proctologists keep up with the pace of advanced surgery. The reason we have not done so with hæmorrhoids is that bugbear, hæmorrhage. It is nothing more, but it is hard to imagine a surgeon of to-day becoming panic-stricken at a hæmorrhage from some comparatively small blood-vessel. If we keep our wits about us, who cannot control a hæmorrhage such as we may find in the hæmorrhoidal region? We have read so much about the subject, that we become panicky when we see a hæmorrhage in this region. I would

rather give a warning about infection, for it is harder to control.

Another obsolete usage is the "rectal plug," which produces hæmorrhage rather than controls it. Muscular contraction is the thing to depend upon in controlling hæmorrhage, whether it be the sphincter or the minute muscularis mucosa. When all muscles are contracted, the hæmorrhage stops. The rectal plug is against muscular contraction, and besides is barbarous, for nothing is more painful.

Why constipate our patient? That is not modern surgery; toxic absorption is against repair. With proper use of the enema, we can move the bowel with little discomfort to the patient, and how very differently this patient feels than one full of toxæmia. That old "malarial symptom," which we ridicule to day but which the physician of yesterday recognized if he did not explain correctly, is gone. We often hear of some nerve bugbear, but to-day toxæmia explains much.

Why not in this hæmorrhoidal region treat a tumour, as we should in any other part of the body? Excise it, so that the skin or mucous edges come together smoothly. It may be said it takes skill, but then it takes skill to become a modern surgeon. One with a mechanical eye that is able to cut clean. I have little use for the trimmer, "trimmed up all round" quoted by Sir James Goodhart. Let us leave the remaining tissues with as little injury as possible, so as to obtain the quickest possible repair. For this reason, we should avoid the suture when possible. For the internal hæmorrhoid, the muscles will coapt the parts if it has been properly removed; externally, where the wound gapes too much, it sometimes becomes necessary to use the suture moderately. Do not let our experience lead us backwards rather than forwards with the trend of surgical improvement.

REPLY.

(1) By IVOR BACK, M.A., M.B., B.C., F.R.C.S

Assistant Surgeon to St. George's Hospital; to the Grosvenor Hospital for Women, etc.

THE article on "Hæmorrhoids," which I published in the

October, 1914, number of THE PRACTITIONER, was intended to be, among other things, a critical review of the present position of the various methods of treatment of internal hæmorrhoids. In the December, 1914, number, Sir James Goodhart, in an article entitled "On the Injection Treatment for Hæmorrhoids," referred to my paper in flattering terms, for which I am indeed grateful to him.

The fact that so eminent a physician should venture into the realms of surgery, and that he should so strongly advocate the claims of the injection treatment, which, whatever its merits or demerits, is not practised, so far as I know, by many surgeons in this country, has naturally excited proctologists, and has renewed the interest of the profession in this line of treatment. I did not claim to be putting forward any flagrantly new ideas, as those who read my article could see for themselves. Had I at that time known that the injection treatment was first introduced to the medical profession in this country by Mr. Swinford Edwards, I should have acknowledged the fact. But the discussion that my paper has provoked proves it to have served at least one useful purpose.

What pleased Sir James was, that the first treatment I described was that by injection.

In self-defence, I must say that because I described the injection treatment first, I did not mean to imply that it was necessarily the *best* treatment. In proof of this, I beg leave to repeat the final phrase of my first paper: "I look on the results of the ligature operation, *if it is carefully performed and the after treatment is properly superintended*, as being as near perfection as those of any surgical operation can be expected to be." For some reason, which I have never been able to understand, an operation for piles has come to be regarded as one of the simplest in surgery, and as one which any recently qualified man is quite competent to perform successfully. I wish to declare most emphatically that this is not the case. There are many points to be observed, apparently small, and a knowledge of them is only acquired by experience. It is just these points which make the difference between a successful result and an indifferent or bad one. The same remark applies to the after treatment. I

am glad to find that I am in agreement with Mr. Mummery here.

During the last few months, I have had the privilege of taking out-patients at St. Mark's Hospital, where all patients, who have been operated on for piles, are subsequently examined and kept under supervision for a short time in the out-patient department as a routine measure. My experience there amply confirms my original statement about the ligature operation.

To return to the injection treatment, discussion leads to the dissemination of knowledge, and I learn with interest that other surgeons inject all the piles at one sitting. As a matter of fact, I was gradually arriving at this point myself. I began by injecting one pile at a time, and hesitated to do more for fear of that very complication, the possibility of which Sir James Goodhart suggests, embolism. I have never known it occur after the injection of a single pile, and I think it fair to presume that it is equally unlikely to do so after the injection of, say, three or four at one sitting. In future, I shall certainly adopt this modification of my technique.

I can see no reason why the injection of a chemical reagent should cause embolism. To my way of thinking a more likely complication, though I have never met it, would be a thrombosis spreading up beyond the desired area. Since the injection aims at setting up a thrombosis, which is local and confined to the area of activity of the chemical reagent, such a complication is only likely to occur from faulty technique, either from the injection of too large a quantity or of too strong a reagent, or, last but not least, from imperfect asepsis. Sepsis does, as we know in all branches of surgery, cause a spreading thrombosis; most rectal surgeons have seen it in cases of prolapsed strangulated piles which have become infected through their abraded surface. Undue thrombosis is therefore a complication which can be guarded against *absolutely*. With regard to technique, the choice of injecting the piles when extruded, as Mr. Edwards advocates, or through a proctoscope, as I prefer, is an individual one. But I would remark that the cases in which the injection treatment is most likely to succeed, are those less severe ones in which the patient cannot prolapse the piles at will.

The real question which has been propounded by Sir James

Goodhart is, as I take it, not whether injection is absolutely better than operation, but rather whether proctologists in this country resort immediately to operation in cases in which injection would give an equally good result with less inconvenience to the patient.

The orificial expert is fair game for the shafts of the witty. I have seen him accused of losing his head in an attempt to survey the whole field of surgery through the narrow limits of his special aperture! I therefore answer with caution, lest it be said that my enthusiasm has run away with my judgement.

I *do* think the injection treatment has great advantages *in selected cases*, but it has drawbacks as well. The best way of arriving at a sound judgement is to review the *pros* and *cons* categorically.

PROS.

(1) Time is saved. The patient is kept away from his business or duties *at the most* for 24 hours after each injection.

(2) No anæsthetic is needed.

(3) The treatment is painless.

(4) Immediate relief is given.

(5) The risk of complications in skilled hands is, as I have pointed out, nil.

CONS.

(1) It is absolutely contraindicated, as I said in my original paper, in strangulated, sloughing, or irreducible piles.

(2) It is a waste of time, as Mr. Edwards points out, when the piles are complicated, as they so often are, by fissure, fistula, or ulcer, since these can only be cured by operation.

(3) Recurrence; and this is the crux of the whole matter, because it is so difficult to give exact figures on a percentage basis. My own belief is that about 40 per cent. of suitable cases are absolutely cured by the first injection or series of injections; that the remaining 60 per cent. have a return of symptoms within four years; and that of this 60 per cent. another three-quarters are cured by a second injection or series of injections; that is to say, that of the original 100

cases, a permanent cure will not be obtained by injection in 15 cases.

(2) By SIR JAMES F. GOODHART, Bart., LL.D., M.D., F.R.C.P.

Consulting Physician to Guy's Hospital, etc.

THE Controlling Editor of THE PRACTITIONER having kindly allowed space for a few additional remarks upon the foregoing papers, I may first say that I am pleased to have raised the question of the value of injecting piles for their cure, seeing that it has called forth so large a measure of agreement from such acknowledged masters of their craft as Mr. Swinford Edwards, Mr. Lockhart-Mummery, and Mr. Ivor Back. They speak from an experience to which, of course, I cannot pretend, and in comparison with which I have no claim even for an audience, so I shall only venture to enlarge still further on two points, and I would do this almost forgetting my calling for a moment and speaking from the point of view that might be taken by the patient troubled with hæmorrhoids.

One concerns itself with pain. It may quite reasonably be in doubt whether surgery is considerate enough as regards the production of pain and its results. To say this, after these years gone by spent in the continual pursuit of the safest and best anæsthetic, might seem nonsense, but it is not so, for the question here is between a treatment that is *painless* and one that is *not so*, and where the latter has far the greater vogue.

I heard it said the other day that any and every operation is an outrage upon nature. This was no mere reckless emotional statement, for it was intended to convey that every operation acts with more or less vigour as a shock to the body. This is true. In such a matter the rectum may be said to be one of our uncomely parts that have more abundant comeliness, for the extraordinary and concentrated sense, and *special* sense, that harbour round the anal ring are liable to inflict shock on the system to quite a disproportionate degree. I remember paying a friendly visit to an old sailor just after the bowels had acted for the first time after his operation, and I found him reduced to a complete worm and no man ; but as sure as I introduce this subject to A or B, I am waived off the field

with polite contempt, and told that the operation was badly done as "we never get any pain nowadays." But I don't know, I don't know, as the Spring Chicken used to sing. At any rate, this particular operation was done by probably the best known man in his branch of work of that day. The "no pain" of the operator too often means, in the memory of the sufferer, very considerable discomfort and even distress, and we know that the operation for piles, reckoned quite one of the smallest of surgery, is liable to be succeeded by a degree of shock from which recovery may be but slow. I should much like to obtain from the patient's side the percentage of those who call themselves well after a fortnight, or even three weeks. I doubt if it would be a large one.

A method, then, that even those who have gone through it allow to be painless, and that does not take a man or woman from work, has such a commanding advantage that the occasional necessity for a repetition of the treatment seems but a trivial drawback.

I note that the necessity for the selection of cases is insisted upon rather forcibly, even by those who admit a good field for the usefulness of injection, and, of course, this goes without saying; but I would repeat that I have certainly been surprised at the wide area this selection may be held to cover, and in how many grades of severity injection may be quite successful. A word needs also to be said about the after-results in the two groups of cases. I have often wondered whether the operator by knife, ligature, or cautery, when he calls his case well, visualizes to full extent the discomforts that I should suppose, from what I have seen, are not infrequent long after the patient is supposed to be cured.

Post-operative discomforts of defæcation must surely be not uncommon from a variety of conditions. For instance, I think of a thin membranous stricture as one of these, that I have several times come across by accident when attempting to clear up a diagnosis by an examination of the rectum. Indeed, I remember at one time inclining to believe that one particular operator, now long dead, was prone to produce this state, and I think that ligature was the procedure he always adopted. The existence of scar tissue and the doing away with the buffer surface 'twixt skin and mucous membrane are others.

I am quite alive to, and admit the justice of, the criticism that I can know but little of the frequency of such conditions, but I counter it by saying, what I know to be in some measure true, that if I with a very limited field of observation have seen even this little, there must be plenty of others who have seen a like amount under but similar opportunities, and that the information thus obtainable, could it be capitalized, would be by no means negligible. I do not happen to know of any ill effects after injection, save, as has been mentioned in some of the foregoing communications, that it is liable to be incomplete, but I do not write to advocate it as applicable to every case, it would be a poor service to a good operation to claim it as a panacea. I only say, that it is a valuable means of treating hæmorrhoids that is not resorted to so often as it should be.

Perhaps I may be allowed to add that Mr. Ivor Back, in his reply, has treated all points with such impartiality, that one cannot take any exception to his statement of the whole case.

To the editor of the St. Louis *Proctologist*, I must make so bold as to say that I think for the moment he had slipped off his chair. He considers that the ligature, clamp, cautery, and the Whitehead operation are my ideals. If I had an ideal at all, it was, and is, injection. What the editor of the *Proctologist's* ideal is he does not leave us in doubt. It is "a surgeon who with a clear eye cuts clean," and, in so stating his position, he reminds me of one of his compatriots, who once wittily remarked that we no longer removed the tumour from the patient, but accomplished the removal of the patient from his tumour. In other words, he adopts the attitude of pure militarism or the rant of the knife.

SOME CEREBRAL PARALYSES OF "URÆMIC" ORIGIN.*

By H. BATTY SHAW, M.D., F.R.C.P.

Physician to University College Hospital and to the Hospital for Consumption and Diseases of the Chest, Brompton, S.W., etc.

SOME words of apology are needed in introducing such a subject as this. In the first place, it would be very difficult to say what is meant by uræmia; and in the second, it would almost seem an impertinence to discuss the forms of paralysis which occur in such a condition, when they are so well recognized in the text-books and systems of medicine. It will, doubtless, be surmised, however, that there is something special in the nature both of uræmia and of some of the paralyses about to be discussed, which has attracted the attention of the writer. This is a fact, and it depends upon a certain dissatisfaction which is constantly felt, when theories have been found wanting, and physical signs have turned out to be fallacious. A paper such as this, affords an opportunity for practitioners to measure their practical knowledge, and to see how much or how little theoretical considerations are in harmony with it.

URÆMIA.

The very word seems to carry in it all that can be wanted to explain it. There is a certain condition found in the patient, which is due to an excess of urea in the blood. But most probably some facts will be present in the reader's mind, and one of them is that he remembers distinctly, that though as a student he was invited to accept uræmia as a definite clinical condition, he was told as well that there was grave reason to doubt whether what underlay this state, was an excess of urea in the blood or a diminution of urea in the urine; that though in some cases these conditions were found, yet in others they were absent. He will remember that some

* The Inaugural Address delivered before the Stoke Newington and North Hackney Medico-Ethical Society.

investigators believed that the real trouble was an excess of ammonia in the blood, and so he was led to believe at last, as other bodies were supposed to be the cause, that after all the cause was not known. It is sad to have to admit that the imperfection in our knowledge as to the actual cause of uræmia is little improved by latter-day investigations. But still there has been some advance, and it is probable that we are nearer the truth than we used to be.

Let us try to see if we can come to some agreement as to what, clinically, we should call uræmia. Probably, we should all think of a case presenting the following features: there is albuminuria, casts are present in the urine, and there is dropsy; in addition, there are headaches, vomiting, an offensive "uræmic" breath, and, if the picture were completed, signs of cardiac hypertrophy independent of valvular lesion, accentuation of the aortic second sound, tortuous brachial arteries, dyspnœa independent of lung disease or pleural effusion, and albuminuric neuro-retinitis. If as well there were a scanty output of urine, coma, and fits, we should fully agree with the diagnosis.

ACUTE AND CHRONIC URÆMIA.

If the symptoms developed rapidly, or came on gradually for a long time, we should speak of acute or chronic uræmia, and we should expect to find the kidneys seriously affected with parenchymatous or interstitial disease, or both. It is commonly thought that the acute and recoverable uræmic cases are dependent rather upon parenchymatous disease of the kidney, especially the acute inflammations, and that such cases are free from the clinical signs of cardio-vascular change. When these latter signs predominate, we should expect to find chronic uræmia and a certain amount, perhaps, indeed, a great amount, of interstitial mischief in the kidneys.

LATENT URÆMIA.

But we are not at the end of the varieties of uræmia, for there is still the "latent" form to discuss, which, curiously, is characterized by the almost complete absence of "uræmic" manifestations. If one kidney is absolutely destroyed, so that the patient has but one organ to depend upon, and if

that one organ suddenly is struck out of function, for instance, by the firm impact of a stone in its ureter, no urine or very little urine is passed. One hears the strange story that the patient has not passed any urine for five days or so; but the patient is found little the worse for this extraordinary condition and may not have a single symptom to complain of except the anuria. Further, he may even go on in this condition for from 9 to 14 days. By that time, perhaps before that time, he may be a little restless, his pupils may become contracted, and he may show a little alteration of the pulse, slight muscular twitchings, a little nausea, and a little headache. This most dangerous condition we speak of as "latent uræmia," and unless we are fortunate enough to discover the kidney which, though not able to function by reason of the calculus or other obstruction, could do so if relieved by the proper operation, we know the patient will certainly die.

ACUTE OR CHRONIC "URÆMIA" IS REALLY URÆMIA ADDED TO SOME TOXIC BLOOD STATE.

Even on clinical grounds, we have every reason to wonder why there should be such a difference in the pictures of acute and chronic uræmia, as opposed to latent uræmia; the former are so well manifested by obvious symptoms, and the latter so characterized by their absence. One doubts very much whether we understand what uræmia is, and our doubts are thoroughly justified. A patient suffering from anuria, due to non-obstructive suppression of the functions of the kidneys, reveals a picture so full of details easily recognizable; whilst the patient suffering from anuria due to obstruction of the ureter, from whatever cause, gives almost no picture at all. The former patient dies in three or four days; the other may live, may be, for a fortnight.

I submit that, if the symptomatology of uræmia depended on the inability of the kidneys to excrete various metabolites, such as urea, ammonia, or any allied body, the clinical pictures in the two conditions should be identical. They are not identical, and we have every reason to believe that it is not so much that the kidneys are at fault in both, but that in one case there is a pre-renal abnormality, and in the

other none. In non-obstructive suppression of urine leading to the classical picture of uræmia, the abnormality producing both the uræmia and, perhaps, the kidney disease, must be an abnormality of the blood. In obstructive suppression of urine with little or no uræmic manifestation, the one and only cause is the kidney disability. When that is relieved the slight symptoms present rapidly disappear, showing that the blood in this case, though clearly charged with metabolites which ordinarily escape by the kidneys, is little damaged.

In short, the very condition least like clinical "uræmia" is produced by a condition of the blood, which is most truly full of urea and the other metabolites associated with it, but with no other abnormality so far as we know; whereas, the condition, which gives us the most faithful picture of what we call clinical uræmia, is just the one in which urea and its allies, though sometimes retained in the system, are not responsible for the uræmic symptoms. What we clinically call "uræmia" is, in truth, a something else added to a pathological uræmia.

THE CAUSE OF URÆMIA.

Do we know what this something else is? Has experimental medicine defined the effects produced by this something else? Well, to such questions, two facts may be brought forward. One is, that in a great number of the cases, perhaps all we call acute and chronic uræmia, the blood-pressure, temporarily or permanently, is raised; the other is, that in the same cases, so far as has been investigated at present, a considerable number show a reduction of the alkalinity of the blood. These are the two facts which have come to the front in the last decade or so.

It will be observed that we have not learnt of the presence of any new body in the blood in these cases; what we have learnt is, that there is a change of the functions of the blood. The blood has assumed more "pressor" characters, and become less alkaline. In short, its physiologico-chemical character is altered, but not in accordance with the older views, for those simply asked us to believe in a quantitative change of crystalloid metabolites. These were simple bodies, which, it may be added, had by Nature been derived

from some complex bodies, and which experiment has shown are of little harm to the body, even when, as in the case of obstructive suppression of the urine, they were accumulated in large quantities in the body. There may be, however, a limit to the degree of retention which can be tolerated, for, as we know, death does occur, even though it be so late as the 14th day of retention; but we are not sure that death is due to the mere retention of urea, and it may be due to some other body. It may rightly be asked, what is the cause of the increased "pressor" character of the blood, and what is the cause of the decreased alkalinity of the blood, which seems to underlie uræmia?

ACIDOSIS.

It is easier to answer the latter than the former question. Death from chloroform poisoning and death from puerperal eclampsia have shown us, that the parenchyma of the liver especially and of other organs may reveal marked degeneration; a reduction of the alkalinity of the blood in these cases has been attributed to the liberation from the parenchyma of these organs of acid bodies, by way of the disintegration of proteids.

Further, we know that a reduction of the alkalinity of the blood is a common feature in diabetic coma, especially when we follow the older and now discredited method of cutting off from our patients all carbohydrates, whereby we compel the patient to burn up his own proteids and fats, for he has no carbohydrates stored up. Here again, the destruction of fat has led to the liberation of glycerine and fatty acids, and the latter bring about the reduction of the alkalinity of the serum —a relative acidosis, as it is described—and diabetic coma may result.

We may not be so sure why acidosis is present in uræmia, but it is not too great a guess to believe that it is brought about by some proteid change; for the alveolar carbonic acid gas sinks in uræmia, and the fact, that cirrhosis of the liver may produce in the patient uræmic symptoms almost identical with those of kidney disease, supports the idea. But other facts have recently been discovered by the analysis of the blood in cases of dyspnœa, a common sign in uræmia,

and I have known cases of dyspnœa to be associated with uræmic breath, and even with convulsions, which, so far from being found to be due to renal disease, were proved to be associated with quite healthy kidneys. Such dyspnœa may merely depend upon a diminished power of the blood to take up oxygen, according to the theory of Barford and his pupils. The blood is said to be "meionectic."

HYPERTENSION. RENAL AND PRE-RENAL CAUSES.

The association of hypertension with uræmia is a harder problem, and awaits its final solution. At one time, I believed it was always dependent upon the entrance into the circulation of kidney tissue, which is known to be "pressor" in action (*see* Chart No. 1).

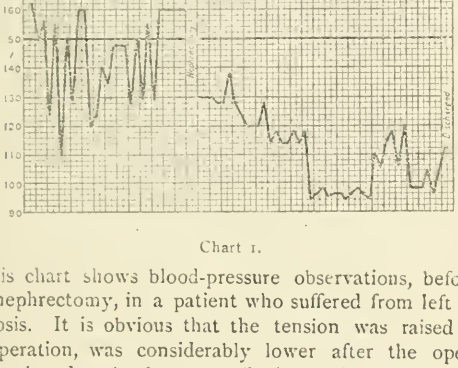

Chart 1.

This chart shows blood-pressure observations, before and after nephrectomy, in a patient who suffered from left hydronephrosis. It is obvious that the tension was raised before the operation, was considerably lower after the operation, and continued to be lower until the patient passed out of observation on being discharged quite well. It really looks as if the atrophy, which was taking place in the left hydronephrotic kidney, had led to the entrance of renal tissue into the circulation causing the rise of tension. When the faulty organ was removed, the raised tension gave place to normal and subnormal tension.

To my chagrin, I have seen cases of high blood-pressure

associated with little or no change in the kidneys. Evidently, in some cases, then, we must look for pre-renal causes.

Thus, the two more recently discussed alterations of the blood in kidney diseases may be due to causes outside the kidneys and independent of them. We may feel that such an explanation is most revolutionary, in that it upsets all accepted doctrines. However, it is no use avoiding the difficulty, if the accepted doctrines have always been held to be of doubtful value, and if the facts of bedside study give the lie to them. Neither urea nor any other crystallizable metabolite is capable of causing hypertension; indeed, they produce hypotension, and, so far as I know, do not cause a reduction of the alkalinity of the blood.

NEED FOR RETAINING THE TERM "URÆMIA."

In the absence of knowledge as to the nature of the causes which produce hypertension and acidosis, we may keep the term "uræmia" as one which describes a fairly definite clinical state. But we must be open-minded about it, and when next we meet with what looks like uræmia, we must see to it that we have as well, definite evidence of disturbance of the kidneys, such as albuminuria, dropsy, casts, and albuminuric neuro-retintitis, before we state that the uræmia we are called upon to help is associated with kidney disease.

I have seen "uræmic" manifestations in liver diseases and in cardiac failure; yet the kidneys at the post-mortem were found to be practically healthy. If we admit that "uræmic" manifestations may be present when all seems well with the kidney, judging either from the clinical or pathological point of view or from both, a point which I think may be conceded, then the way is open to discuss the cerebral paralysis which we may meet with in this anomalous condition.

URÆMIC CEREBRAL PARALYSIS.

I do not propose to discuss all the causes of cerebral paralysis, which we meet with in uræmia, for they are well enough known. We have all seen the commonest cause, namely, cerebral hæmorrhage, most frequently into the in-

ternal capsule, and, though less frequently, into the meninges. But a point which is of interest is this, that we may not rely on the blood-pressure chart as a means of diagnosis of cerebral hæmorrhage from other causes of cerebral paralysis, such as thrombosis, embolism, meningitis, etc. (which may be the causes of cerebral paralysis in uræmia), in cases showing hypertension.

A large cerebral hæmorrhage will, on its own account, cause high blood-pressure, but, unfortunately, uræmia is in itself frequently associated with hypertension without the occurrence of cerebral hæmorrhage. To put it in another way, a patient who has had an attack of hemiplegia, and is found to have high blood-pressure, may owe his high blood-pressure to a hæmorrhage, to the state we call uræmia, or to both. This brings us to the form of cerebral paralysis occurring in uræmia, *which may be unassociated with any visible naked eye change* in the brain whatever. This is the form of cerebral paralysis to which I wish to call attention, especially because it is one with which we are least familiar, and about which, though recognizing its existence, we have so little to say in explanation.

Let us turn to the various nervous manifestations with which we are all familiar in uræmia. The more common group is that which shows that the cerebrum and other nerve centres, so far from being paralysed, are irritated, namely, uræmic convulsions or epilepsy, uræmic mania, uræmic delirium, uræmic delusions, uræmic vomiting, uræmic dyspnœa. It is quite clear that both the cerebral cortex and various nerve centres are capable of being irritated, until one or other of the above manifestations is brought about. What is it that causes this irritation? All we can say is that the blood in at least one of them—uræmic dyspnœa—shows reduction of alkalinity. As to the other manifestations, we are completely ignorant of their causes, or of any associated change in the blood. We know, from what has already been said, that it is not due to the retention of any known, crystallizable body. I have admitted that there is no satisfactory direct evidence to prove that it is always due to any effect of the kidney substance, which has been diverted into the blood stream. All we can say is, that it is due to some

abnormal substance present in the blood.

But we must turn to the obverse, and remember that just as uræmia may be associated with signs of irritation of the central nervous system, so it may be associated with signs of depression of the nervous system, including the cortex and nerve centres. For we are all familiar with uræmic coma, uræmic melancholia, or other forms of uræmic insanity of a depressed type, with uræmic apnœa such as we see in Cheyne-Stokes breathing; lastly, we may or may not be familiar with the subject of this address, uræmic cerebral paralysis, hemi- or monoplegia, uræmic aphasia, and uræmic blindness.

UR.EMIC CEREBRAL PARALYSIS *versus* PARALYSIS FOLLOWING THROMBOSIS OF THE CEREBRAL VESSELS.

I will now ask what is our position, when a patient is brought to us, who, without losing consciousness, has become paralysed down one or other side, the paralysis coming on slowly or with moderate rapidity, and who eventually loses all signs of paralysis? In the absence of any pain or any signs of kidney disease, such as albuminuria, dropsy, or casts in the urine, I think I am right in saying that we should attribute it to thrombosis of the arteries of the brain. If such attacks are repeated, and equally well recovered from, we should adhere to the same opinion. Indeed, some of us, in obedience to past faulty teaching, may say that the condition, even if repeated, is due to recurring hæmorrhages, a position hopelessly wide of the mark. How can a cortex or pyramidal tract be damaged over and over again in its structure, *and as often recover?*

No, it is most likely we should say that it was due to thrombosis of the cerebral vessels, and that the recovery was due to collateral circulation supplying the affected nervous substance with a proper amount of blood. Some of us even would still be inclined to be critical, and wonder whether a thrombotic hemiplegia could possibly be recovered from *several* times, each time being due to thrombosis. I now show blood-pressure charts of two cases (Charts 2 and 3), both of whom were admitted for hemiplegia, and both of whom recovered from the hemiplegia before they left the hospital.

There is now a greater inclination to agree that hypertens-

ion is an expression of toxæmia, and not of arterio-sclerosis. No doubt, stiff vessels may cause the sphygmomanometer to

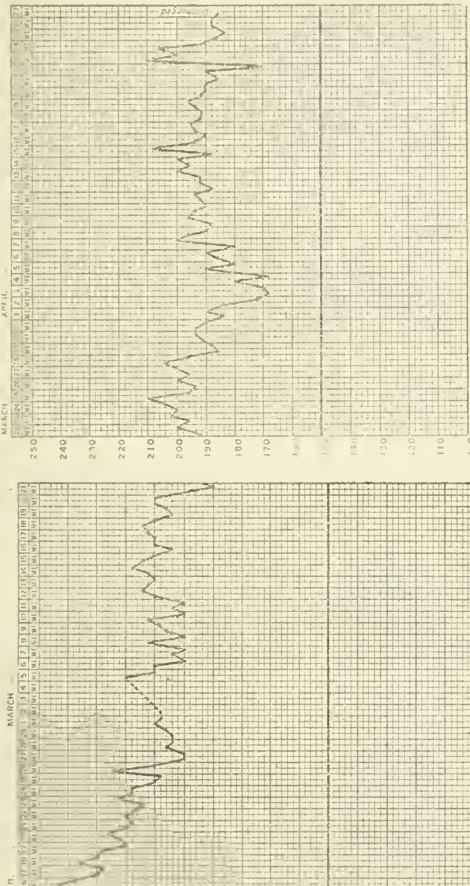

Chart 2.—*Thomas R., æt. 50, Milkman, admitted for right-sided hemiplegia, which was recovered from before discharge from hospital; albuminuria; note gradual fall of pressure with rest in bed.*

give a reading of 150 mm., but one of these cases showed a reading of 198 mm., and the other of 244 mm. We have

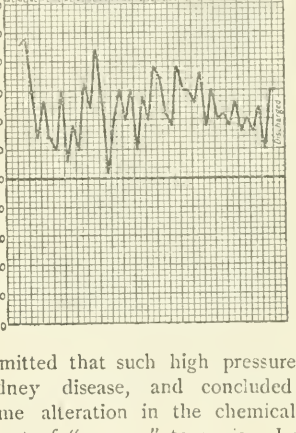

Chart 3.—*Alice G., æt. 53, admitted for "tingling and numbness" of right face, arm, and leg, also for paralysis of the same parts; deep reflexes not increased; extensor plantar response on right side on admission, became flexor on November 9, no albuminuria (four examinations), few hyaline casts in urine, arteries tortuous, aortic sound accentuated. Complete recovery from hemiplegia on discharge.*

admitted that such high pressures do not necessarily mean kidney disease, and concluded that they might mean some alteration in the chemical character of the blood—a sort of "pressor" toxæmia. I admit that I do not know for certain that neither of these cases owed the hemiplegia to thrombosis of the cerebral vessels, but almost certainly they did not owe it to hæmorrhage, for they both recovered completely.

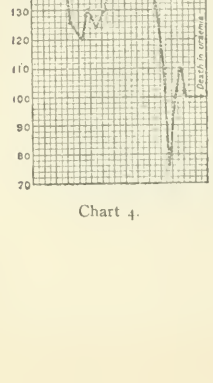

Chart 4.

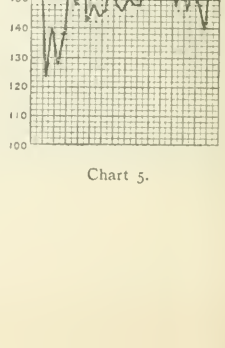

Chart 5.

But what we do know is that syphilitic or other infective thromboses of the cerebral vessels are not causes of hypertension ; these two cases showed hypertension, so that it is presumptive evidence that the hemiplegia was not thrombotic.

With regard to the next charts (Charts 4 and 5), one of the patients (Chart 4) was admitted to hospital for loss of strength, shortness of breath, and partial loss of consciousness ; the urine was free from albumen, and his pressure had reached as much as 160 mm. He died, and was found to have granular kidneys. Death was accompanied by symptoms of uræmia ; but the point of the case is that two years previous to admission he had had a stroke, producing left hemiplegia, from which he recovered. At the post-mortem, no sign of any alteration of the brain or cerebral vessels could be found to account for his former hemiplegia. It is true he had had syphilis, but no sign of any syphilitic scar or of occluded vessels in the brain could be found. Presumably his cerebral paralysis, which had been entirely recovered from, was due to a previous attack of so-called "uræmia."

The case of the other patient (Chart 5) was more convincing still. He was an elderly man, æt. 80, who was noticed to reel and almost to fall in the street. He was brought to the hospital, and, though he had not lost consciousness, was found to have left hemiplegia, hypertension, and albuminuria ; both knee-jerks were exaggerated, and the plantar response of the left foot was extensor in type. Up to the time of his seizure, he had had no illness whatever throughout his long life. His hemiplegia persisted, and on the eighth day after admission he died. He had hypertrophy of the heart, which weighed 16 ozs., and his kidneys were granular and only weighed 4 ozs. each. There was absolutely no sign of disease in his brain or cerebral vessels ; everything appeared to be normal, even when the brain was hardened and subsequently laid open. Here is absolute proof, then, that uræmia, in this case an admittedly unique form of it, or, at any rate, hypertension and granular kidneys were accompanied by a hemiplegia which was apparently unaccompanied by any change in the brain or cerebral vessels. There must have been some poison or poisons circulating in his blood, which caused his hypertension and the paralysis which *so closely simulated an organic*

one, for he had an extensor plantar response on the affected side. For those who have never seen or heard of such a case, here is one proved up to the hilt.

THE IMPORTANCE OF RECOGNIZING THE EXISTENCE OF URÆMIC CEREBRAL PARALYSES.

Turning now to the practical side of the question, it is this, that we must not only think of a thrombotic hemiplegia in future, with all the elements of a wrong prognosis following in its wake, if we find hemiplegia occurring in a case of uræmia or hypertension. We may say that the patient may get quite well of the hemiplegia, but we cannot say for certain. The same may be said of cases of recurrent loss of consciousness associated with uræmia or hypertension.

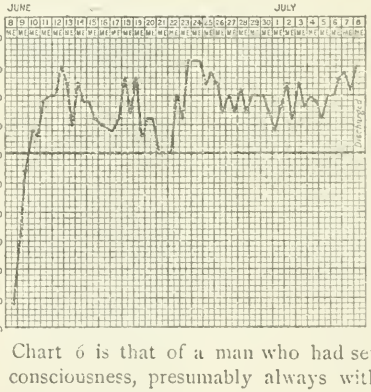

Chart 6.—*James B., æt. 50, Taxi-cab driver, admitted unconscious, but recovered and was discharged spree from signs and symptoms except the raised blood-pressure. Wassermann test negative. He had previously lost consciousness on several occasions.*

Chart 6 is that of a man who had several attacks of loss of consciousness, presumably always with hypertension; yet he recovered each time.

Not only may parts of the cortex, associated with movement or the conscious state, be thus affected, but even the occipital lobes as well in such cases (Chart 7). The patient was so blind that he was unable to count fingers held close to the eyes; yet neither occipital lobe showed any change post-mortem, and there was a very small amount of neuro-retinitis.

THE EXPLANATION OF URÆMIC CEREBRAL PARALYSES.

What, then, is the explanation of such curious paralyses?

They are almost certainly of toxic origin, and the toxin picks out motor areas in one individual and sensory areas in another. We do not know why it should be so selective, any more than we know why arsenic should pick out one set of nerves, lead another, and diphtheria another; nor do we know why one cerebral cortex should be singled out for attack in uræmia more than the other, any more than we know why lead should do the same thing.

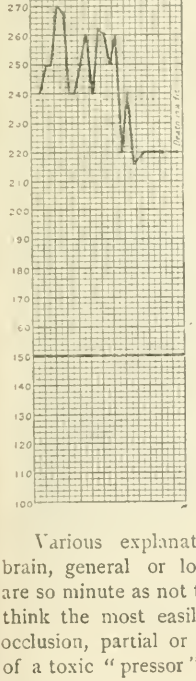

Chart 7.—*Frank O., æt. 38, Coach-painter, admitted for blindness which was so intense that he could not "count" fingers," held up close to his face, loss of all sense of colour, also headache and vomiting, previously in hospital two years ago for uræmia and hypertension. Fundus of each eye showed albuminuric neuro-retinitis but not marked enough to account for the extreme blindness, and, moreover, the sight improved considerably a few days before death in a fit; albuminuria but no casts found during life.*

Various explanations have been given: œdema of the brain, general or localized, and minute thromboses which are so minute as not to be recognizable; but of all the causes I think the most easily understood is anæmia from temporary occlusion, partial or complete, of the vessels. The presence of a toxic "pressor" body in the blood, which appears to be so often the case in uræmia, makes it easy to understand that such a body acting on the brain vessels would cause them

to contract. If the arteries going to the particular area of the brain affected are small, then a moderate contraction of them will produce a relatively greater anæmia of such parts than of other parts of the brain, and they suffer to the exclusion of the others. Experimentally, such a possibility has been found non-existent in animals, in whom the cerebral vessels have no neuro-muscular control. It does not follow that the cerebral vessels of man are free from such control; indeed, it has been shown that there is a vasomotor apparatus in the cerebral vessels, though it is true that it is not a very perfect one.

One last word, and it is this: if uræmia and its various manifestations are associated with a pressor toxæmia and acidosis, then venesection and the use of alkalies by intravenous or subcutaneous infusion should give us the best results in such cases.

That recovery may take place with rest and simple treatment is shown by the fact, that a pressor toxæmia is present and can pass off spontaneously as seen in Chart 8

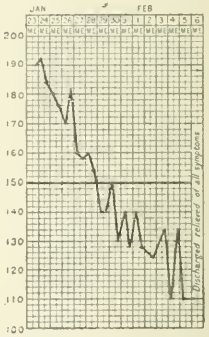

Chart 8.—*Charles A., æt. 33, Carman, admitted for dropsy. Albuminuria, tortucus brachial arteries. With the fall of the pressure with rest in bed, the dropsy disappeared, and the patient was discharged free from all symptoms.*

of a patient in whom, with the disappearance of symptoms, there was a disappearance of the high tension.

FOUR CASES OF INCIPIENT PULMONARY TUBERCULOSIS IN CHILDREN.

BY D. B. LEES, M.D., F.R.C.P.

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THE following four cases were included in the Address with which I had the honour, as representing the section of Medicine, of opening a discussion in the combined sections of Medicine, of Diseases of Children, and of Electrotherapeutics and Radiology, on the Diagnosis of Chronic Pulmonary Tuberculosis in Infancy and Childhood, at the Aberdeen Meeting of the B.M.A. last July. The four cases, however, did not appear in the published abstract of my paper (*B.M.J.*, September 12th, 1914), and as I specially requested that those who listened to me would read them carefully when they appeared in print, because they illustrated and enforced the more important details of my Address, I now publish them separately in THE PRACTITIONER.

The first of these cases demonstrates the importance of percussion-evidence, and of deficient entry of air, even though no morbid sounds can be heard on auscultation.

The second illustrates the production of asthenia in a young child by enlarged tuberculous bronchial glands.

The third was complicated by spinal caries.

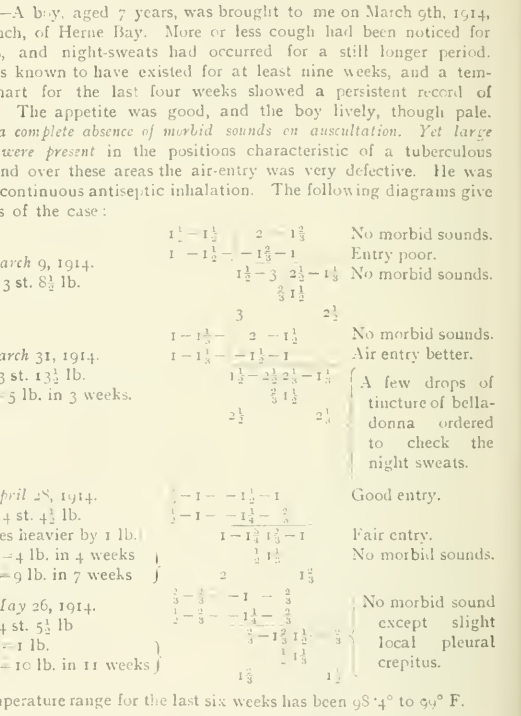
The fourth demonstrates the possibility and the importance of detecting the very earliest indications of tuberculosis of lung and bronchial glands, when one lung only may be implicated.

All four cases were treated by continuous antiseptic inhalation, and all made a good recovery.

In the diagrams which follow, the upper part shows the front view of the chest, and indicates the size of the dull pulmonary areas in the inner and outer parts of the first and second intercostal spaces on each side; while the lower part shows the back view of the chest, and indicates the size of the areas in the inner and outer parts of the supra-scapular fossa, and that of the lower lobe dull area on each side at the extremity of the scapular spine, as well as of the dull areas close to the spine at

the 3rd dorsal level caused by enlarged bronchial glands. The figures are in finger-breadths and fractions of a finger-breadth.

Case 1.—A boy, aged 7 years, was brought to me on March 9th, 1914, by Dr. French, of Herne Bay. More or less cough had been noticed for six months, and night-sweats had occurred for a still longer period. Pyrexia was known to have existed for at least nine weeks, and a temperature chart for the last four weeks showed a persistent record of 99°–100° F. The appetite was good, and the boy lively, though pale. *There was a complete absence of morbid sounds on auscultation. Yet large dull areas were present* in the positions characteristic of a tuberculous infection, and over these areas the air-entry was very defective. He was treated by continuous antiseptic inhalation. The following diagrams give the progress of the case:


No morbid sounds.
Entry poor.
No morbid sounds.
No morbid sounds.
Air entry better.
A few drops of tincture of belladonna ordered to check the night sweats.
Good entry.
Fair entry.
No morbid sounds.
No morbid sound except slight local pleural crepitus.

March 9, 1914.
3 st. 8½ lb.

March 31, 1914.
3 st. 13½ lb.
Gain = 5 lb. in 3 weeks.

April 28, 1914.
4 st. 4½ lb.
In clothes heavier by 1 lb.
Gain = 4 lb. in 4 weeks
Total gain = 9 lb. in 7 weeks

May 26, 1914.
4 st. 5½ lb
Gain = 1 lb.
Total gain = 10 lb. in 11 weeks

The temperature range for the last six weeks has been 98·4° to 99° F.

July 8, 1914.
4 st. 9½ lb.
Gain 4 lb.
Total gain = 14 lb. in 17 weeks.

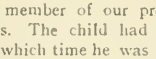
Areas as above. No morbid sounds.
Temperature 99°–100° every day during the last month, yet the boy seems well, is very lively, and growing rapidly.

October 4, 1914
4 st. 13 lb.
Gain = 3½ lb.
Total gain = 17½ lb. in 7 months.

Normal gain in 7 months = 3 lb.

Pulmonary areas smaller than on May 26. Gland areas remain unaltered. Temperature 99°–100° till the end of August, since then it has fallen slowly: lately about 99° F. in the morning and normal at night; for the last two days it has been normal all day. Height and weight much above the average for his age.

Case 2.—On February 28th, 1913, I was asked to see the little son, aged 4 years, of a member of our profession, a colonel in the Royal Army Medical Corps. The child had suffered from "asthma" since he was 2 years old, at which time he was living at Cork, in Ireland. There was never complete remission of the dyspnœa, but it was worse from time to time, and especially at night; these nocturnal attacks were often severe. He had been examined by many doctors, who all stated that there was "nothing wrong with the lungs," and his asthma had been treated with belladonna, with stramonium, and with potassium iodide. I found the boy very wheezy and very thin. His right heart was distinctly dilated. Percussion at once revealed rather large dull areas in the positions characteristic of tuberculosis, and also large dull areas over the bronchial glands. It was not possible to ascertain his weight.

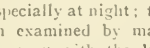


Defective entry at apices.

February 28, 1913. (Incomplete examination.)

Wheezy râles generally.

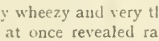
It was directed that he should be kept in bed, and should practise continuous antiseptic inhalation.



Pulmonary areas less. Gland-areas unaltered.

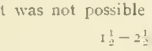
March 7, 1913. Looks a little fatter.

March 14, 1913. Has been quite free from spasmodic dyspnœa this week. Likes his inhaler.



Areas in front still diminishing.

March 28, 1913. Had a bad dyspnœic attack during the night of March 17th–18th, and smaller attacks for two or three nights after; but no such attack during the last week. Child is very lively, and plays eagerly, wearing his inhaler all the time.



Areas all a little smaller.

After this I saw him no more until August 9th, 1913, when he was brought to my house. There had been only one attack of asthma during the last three months. Several months later, his father reported that the boy was quite well and very lively, without any asthma for months past.

Case 3.—A little girl, aged 3 years and 9 months, was sent to me October 12th, 1912, by Dr. French, of Herne Bay. She had suffered from scarlet fever in August 1910; this was followed by otorrhœa, with offensive discharge, which continued until a mastoid operation was per-

formed in March 1912. Soon after the scarlet fever she had stiffness in the limbs, with tenderness and some swelling of the knees. Since December 1911, it had been observed that her neck was stiff, and her cervical glands enlarged. She had been kept in the recumbent position during the last seven weeks.

There was obvious distortion and some tenderness of the cervical spine. She could sit up with head erect, and could move it to some extent forwards and backwards, but hardly at all sideways. There were many enlarged cervical glands on both sides; the axillary glands were also enlarged. Knees and ankles normal. Feet cold. Knee jerks normal. Plantar reflexes flexor. Abdomen distended, tympanitic; no lumps or bands; no ascites. Liver-dullness to two finger-breadths below costal margin. *Spleen felt without difficulty; it was abnormally firm.* Heart normal, except for a hæmic pulmonary systolic murmur. Examination of her lungs showed *a typical series of dull areas in the positions characteristic of a tuberculous infection*, with very defective air-entry in the apical region, but *no definite morbid sound.* The air-entry was much more free at the bases.

It was directed that the recumbent position should be carefully maintained for a period of twelve months, and that the method of continuous antiseptic inhalation should be adopted for several months.

On October 17th, 1913, I saw her for the second time. She had been kept lying down during an entire year, and the *inhaler had been worn continuously for the first six months.* She could now turn her head freely from side to side. The spleen was now normal; the axillary glands not much enlarged; the cervical glands still felt on both sides, but small and discrete. The dull areas in the lungs were all smaller; no morbid sounds.

It was advised that the recumbent position should be maintained for six months longer.

On March 18th, 1914, she looked remarkably well. Head movements normal, except for slight limitation backwards. Glands in neck and axilla difficult to palpate. All the tuberculous pulmonary areas very small. She was now allowed to sit up, at first for half-an-hour daily. Massage of the feet and legs was ordered with passive flexion of the ankles, to counteract a moderate retraction of the heels caused by her long period of recumbency.

Three months later (June 1914) she seemed quite well and was walking freely. No retraction of heels now, but some knock-knee was present, which was found to be due to flat-foot. Surgical soles were ordered for her, and tip-toe exercises. She went on well until the middle of August, when she had a sudden pain about the middle of the chest: the temperature rose to 104°, and some pyrexia continued for a week; also the neck became more stiff. Ten days later she had an itching erythematous rash on the face, body and limbs, which a medical man diagnosed as "urticaria." I saw her again on October 8th, 1914, when I found the lateral movements of the head more restricted than in June, forward movement good, backward movement fair. No deformity. No tenderness, but she had complained of pain in the right neck. Many small shotty cervical glands could be felt. No increase in the pulmonary dull areas. Knock-knee less. R. instep normal; L. instep improved. Walks better. Heart

normal. It was advised that she should be kept lying down, with continuous antiseptic inhalation, for three months.

Case 4.—A boy, nearly 13 years old, was brought to me September 16th, 1913, by Dr. Bowen of Cambridge. In February, 1913, he had a slight attack of scarlet fever, for which he was isolated at school along with another boy, in whose case the scarlet fever was followed by "whooping cough and broncho-pneumonia with much sputum." In April, 1913, Dr. Bowen was asked to examine him, and found some cardiac dilatation, with a booming sound over the right ventricle. The patient was kept at rest, and the cardiac condition improved. At the consultation on September 16th, it was found that the cardiac dilatation was decidedly less, though it was still distinct. There was a faint systolic murmur over the right ventricle. It was thought that no organic disease of the heart existed, and that the boy might be allowed to return to school (on the coast) and permitted to play, though not to take part in organized games

But during the physical examination of his chest we detected *a small area of dullness in the inner part of the first right intercostal space, and a second dull area close to the spine on the right side posteriorly, at the third dorsal level. No dullness elsewhere.* It was thought that this indicated a localized tuberculous infection of the right upper apex and of the right bronchial glands. It was hoped that these evidences of a localized tuberculosis would subside under the tonic influence of sea-air. Seven weeks later, on November 6th, 1913, he was brought again for examination. He looked thin, anæmic, and listless, and was found to have lost half a pound in weight. He had now *dull pulmonary areas in all the positions characteristic of tuberculosis*, and very slight inspiratory crepitus was heard at his right upper apex, both in front and behind. This evidence of a spreading tuberculous infection of the lungs demanded immediate treatment. He was, therefore, not allowed to return to school, but was sent home and kept in bed for ten days with continuous antiseptic inhalation. He wore the inhaler persistently, and when again examined three weeks later (November 27th) he had gained four pounds in weight, and all his dull pulmonary areas were smaller. The crepitus had nearly disappeared, but expiration was distinctly prolonged at the right upper apex posteriorly. On December 18th he had gained two pounds more; the dull areas were still diminishing, but the prolonged expiration at the right upper apex was still audible. On this occasion we had the advantage of consultation with Sir John Rose Bradford. The treatment by continuous antiseptic inhalation was persevered with, and when Sir John Bradford saw him with me for the second time, on April 27th, 1914, there had been a *total gain of ten pounds in six months.* The improvement has been permanent. He is now at a public school, and in good health.

As these four cases have by force of circumstances been separated from the address which they should have illustrated, and as this address may not be in the hands of all readers of The Practitioner, it seems desirable to add a few words to explain why these dull pulmonary areas are

taken to be good evidence of a tuberculous infection of the lungs.

In order to arrive at a sound conclusion from the results of percussion, it is essential that a correct method should be adopted. The inadequate and misleading statements of the text-books with regard to percussion in incipient pulmonary tuberculosis are founded on the examination of patients in the sitting or standing position. This position inevitably leads to false conclusions in the examination of the front of the chest, because it does not allow of complete relaxation of the muscles, or of the counter-resistance which is necessary for even the lightest percussion-stroke.

It is essential that, for the examination of the front of the chest, the patient shall be recumbent on a comfortable couch, and perfectly at his ease. For the examination of the back of the chest he should be in a sitting and slightly stooping posture, with his hands on the front of the opposite shoulders, the elbows together, and the muscles relaxed. The medical man should press firmly with the terminal phalanx of a finger of his left hand on the spot to be examined, keeping all the rest of his hand and arm away from the patient's chest-wall. He should then percuss lightly with a finger of his right hand, and measure in finger-breadths the diameter of the dull areas detected.

In any case of undoubted phthisis, with pyrexia, cough, hæmoptysis, night-sweats, and sputum containing tubercle bacilli, it is possible, except perhaps in the most advanced stage, to detect the existence of a typical series of dull pulmonary areas, which are found in the same positions in case after case. They are for the most part symmetrically placed in the two lungs, but with certain invariable differences caused by the position of the heart, and by the fact that the right lung has three lobes, the left only two. Their position is shown in a diagram in my published Bradshaw Lecture, and again in the Address at Aberdeen. The size of these areas, and the morbid sounds heard over them will depend upon the duration and activity of the disease.

In cases in which similar clinical phenomena exist, but in which no bacilli can be found in the sputum, the same typical series of dull pulmonary areas, in the same positions, can be

detected.

At an earlier stage, when the symptoms are suggestive of pulmonary tuberculosis, but not in themselves conclusive, the discovery of the typical series of dull pulmonary areas is probably sufficient to establish the diagnosis. Simple collapse of lung, which is common in young children, is irregular in distribution, and not arranged in the pattern characteristic of tuberculosis.

Broncho-pneumonia of non-tuberculous origin affects mainly the lower parts of the lungs. A predominant affection of the apical regions is strong evidence for the existence of a tuberculous infection, either present or past. The existence of mixed broncho-pneumonic infection makes the detection of the typical tuberculous areas more difficult in children, but in many cases they may be demonstrated with great ease. In children, they are almost always associated with dull areas over the bronchial glands, close to the spine at the third dorsal level, especially on the right side.

In the early stage of pulmonary tuberculosis, the entry of air is very defective over the typical dull areas, but there may be no morbid sounds; this fact is very likely to cause error in diagnosis. Even at a very late stage, when the areas are large, there may be few or no morbid sounds, as in the case of a girl of 18 brought to me recently only a month before her death. She had been an inmate of a sanatorium for several months, and had been treated with tuberculin, in spite of her increasing emaciation. Careful percussion showed very large dull areas, though no morbid sounds could be heard.

COMMON ERRORS IN DIAGNOSIS.*

By ADOLPHE ABRAHAMS, M.D., B.C., M.R.C.P.

Medical Registrar to the London Temperance Hospital, etc.

THE subject of this paper was suggested by a series of lectures given some time ago, under the auspices of a well-known post-graduate college, by a number of distinguished consultants and specialists. Each had selected his own particular branch, and dealt with the common mistakes which he had encountered, almost invariably, be it added, at the hands of somebody else. The impressions I derived from these 34 lectures—impressions which, I venture to surmise, would appeal to an average member of the profession—I have synthesized and analysed; so that whatever merit the whole may deserve must be given to a large number of distinguished colleagues, *malgré eux*, upon whose shoulders I may similarly repose the burden of any shortcomings. Very little more than the language is mine, and not that in all cases.

It may not be without interest to reiterate that I attended no fewer than 34 lectures, for it may be wondered how and in what way it is permissible to divide the practice of medicine into so many different branches. A small number were mere repetitions, but the large number of specialties which remain afford an interesting side-light upon the present complexity of our professional work

It is hardly protesting too much that three or four decades back such a series of lectures could have been comprised under perhaps half-a-dozen subjects. But to what a degree have we now attained? It is not enough that the naso-laryngeal expert shall deal with this region of the body; the nose has its own errors so clearly defined, that a separate lecture was regarded as necessary. The chest as a specialty has long since passed away; the man on the lungs had no mention of the heart, and even the cardiac specialist exhibited a marked tendency to dichotomy, for a struggle between

* Paper read before the Abernethian Society of St. Bartholomew's Hospital.

displaying his experience as a clinical diagnostician and his skill as a mechanical cardiologist was manifest. So far from abdominal surgery sufficing as an entity, the general surgeon, although allowed his say, was supplemented by a kidney man and by various specialists upon the alimentary tract. For behold! the intestinal tube itself has been parcelled out. Has not the special study of proctology originated? Has not the appendix its special devotees? Are there not surgeons with options upon the large intestine?

All this terrifying display of human knowledge and wisdom makes the prospect for the future still more terrifying. In all sincerity, one asks where will specialization end, or rather how far can it extend? Shall we have men who will confine their enterprise to the Eustachian tube, as today the labyrinth has its faithful adherents? Will there be, perhaps, labio-glosso-lingual specialists? Or will even such a category be too diffuse, and its separate constituents require special consideration?

The specialists who were invited to contribute their lectures were in all cases distinguished; many might be described as eminent, and to two, or perhaps three, the qualification pre-eminent might justly be applied. Yet, although the majority of the lectures were as excellent as the prestige of their contributors would have led one to expect, in many cases the material was bad, and in a few cases almost incredibly bad. One lecturer made more mistakes in orthoëpy and composition in five minutes than most men could have made in six months; a few appeared to have failed entirely to appreciate the principle of their task, and merely elaborated the extreme difficulties associated with their particular subject, or proceeded in detail to discuss the differential diagnosis of extremely rare conditions.

In fact, it is worth while speculating whom one would select as the best type of man to deliver a tutorial lecture of this nature. That he must be a man of fairly considerable experience goes without saying, but the selection of a senior is fraught with a certain disadvantage. The common errors of diagnosis are the ruts over which the inexperienced traveller stumbles, the memory of which will be more vivid to the younger specialist still sufficiently footsore to be wary, than to

the smoothly-travelling automobilist whose comfort obliterates all memory of the weary pedestrianism of his youth.

Any classification of the causes of mistakes must be an unsatisfactory one, since an abundance of overlapping is inevitable. One differentiation which occurs to me is between pardonable and unpardonable errors; the majority, according to my own unfortunate experiences, are to be included under the latter category. But it is obvious that the judgement of what standard of mistake is pardonable or otherwise is an arbitrary assumption, more especially as a venial mistake on the part of one man is an utterly unpardonable perpetration by another.

Mistakes again may be classified under the two headings: things which we miss, and things which we mistake for others; or again into the incomplete observation of facts, and conclusions drawn from inadequate evidence.

But all these categories are too wide for convenient reference. I should like to reproduce one classification which was given by a very shrewd experienced physician, for whom we all entertain the greatest respect. He divided the causes of mistakes under the headings:—

a. Gross ignorance; *b*. Inexperience; *c*. Over-confidence in one's infallibility; *d*. Carelessness; *e*. Over-pressure of work and consequent inability to devote sufficient time to examination.

I intend to utilize this scheme as the basis of my classification. I do not think, however, that anything is to be gained by a consideration as causes of mistakes of such inborn errors of character as apathy, indifference, carelessness, and conceit. In this connection, Sir William Osler's remarks may be recalled: "the physician, like the Christian, has three great foes; ignorance which is sin; apathy which is the world; and vice which is the devil." Is it too much to comprise nearly all causes of mistakes under the condemnation of vice?

I may say that the classification, which I append, is only built up from the details supplied by many authorities. It is a mosaic, therefore, which would not correspond to the

ideas of any one authority, and I have no doubt it could be modified with advantage. At least, I have attempted to make it as detailed as possible.

CLASSIFICATION.

THE CAUSES OF MISTAKES.

A. Before the patient is seen.

Mistakes made before the patient is seen are naturally few, and the method of avoidance is sufficiently obvious.

B. In the management of the patient.

1. Social—*Mistakes in manner or tact.*
2. Clinical—
   - *a. Mistakes due to ignorance.*
   - *b. To errors of judgement.*
   - *c. To obsessions.*
   - *d. From failure to think anatomically.*
   - *e. From failure to think at all.*
   - *f. From a reluctance to accept responsibility.*
   - *g. From incomplete examination.*
   - *h. From inherent difficulties in the case.*

B. 1. SOCIAL.—*Mistakes in manner or tact.*

Sheer bad manners denote without doubt that a fundamental mistake has been committed, that the doctor has mistaken his vocation.

The anamnesis, which often hinders by casting a red herring in one's path, is occasionally of invaluable assistance, and it requires some tact and patience to decide between garrulous imbecility and valuable information. A careless mistake in management, a suggestion of suspicion during the anamnesis puts the malingerer on his guard, or alienates the confidence of the nervous patient. In fact, the fate of the neurasthenic will be sealed in the first minutes of the first consultation. Once arouse his suspicion that you regard him as a *malade imaginaire*, and his confidence is gone for ever. You have, in very sooth, to learn to palpate a patient's sentiments and auscultate his conscience. It is a very great mistake to say

too much too soon. I need scarcely add a warning of the dreadful danger which may quite unnecessarily be run in a case of suspected pregnancy. Again, the doctor is apt to become indifferent through familiarity with disease, and "a touch of diarrhœa" is diagnosed when typhoid fever subsequently manifests itself. Needless to say, the lay mind will not excuse such a change of opinion.

But in this connection, the doctor is verily between the devil and the deep sea; for the over-cautious man is liable to acquire an unenviable reputation as an alarmist, and a diagnosis of a grave condition, which subsequently turns out to be a simple disorder, is criticized perhaps more sharply than an error in the opposite direction.

The same remark about talking too much applies to prognosis, which, although it does not properly belong to this subject, must be introduced, for it is so inextricably bound up with diagnosis. As soon as the diagnosis is out of the doctor's mouth, he is bound to be asked for the probable course and duration. Nobody can lay down rules for this. A man may be a born diagnostician, but only a profound experience can make him a good prognostician; he has to learn the various factors which impart to the human body its remarkably elastic power for recovery, and at the same time the narrowing margin of safety of its organs as they approach the limits of endurance. The same shrewd physician, to whom I have alluded, advises that a complete prognosis should always be avoided. Sufficient for the day, says he, should be our motto, and the star of hope should be kept shining as long as possible.

I suppose prognosis is more difficult than diagnosis, because in the latter one still has Nature in consultation; when it comes to a question of prophecy, the doctor is pitting his opinion against that of the Senior Practitioner.

B. 2. CLINICAL.

a. MISTAKES DUE TO IGNORANCE.

Under this heading, I include the following considerations:

(1) *Gross ignorance.*—It is difficult to select examples which could unquestionably be comprised under such a title. Let me include two actual examples: Overlooking as a cause

of deafness the presence of a large amount of cerumen; and failure to observe that a large pyriform swelling in the abdomen, four days after delivery, was not "acute metritis" but a bladder containing a gallon of urine.

(2) *Ignorance of Fundamentals, though not so extreme as to be labelled Gross Ignorance.*—Ignorance that the surgical complications of tabes occur very early in the disease may be of immense importance, *e.g.*, Charcot's joint, perforating ulcer, gastric crises, and spontaneous fractures; all of which may occur before the appearance of an Argyll-Robertson pupil or the loss of knee jerk.

It is ignorant to diagnose articular rheumatism under the age of two, for at that age it is practically unknown. In this way, scurvy or acute epiphysitis might be overlooked. Again, ignorance of the symptoms of early phthisis is common through the undue attention which is paid to the recognition of *signs, e.g.*, definite apical dullness; whereas, by the time dullness is present, the condition is an advanced one.

(3) *Ignorance of the existence of very rare Conditions* — In a sense, a consideration of rare conditions is out of place in this paper. Nevertheless, it is worth pointing out that, however rare transposition of viscera may be, failure to recognize its existence will lead to humiliating discomfiture. Incidentally, it may be remarked that the tyro occasionally makes a brilliant diagnosis, through his very ignorance of how rare such a condition actually is. It is satisfactory, too, to remember that the doctor's ignorance is sometimes the patient's blessing, in cases in which the only danger is that the condition is found out, and that, whilst it is as innocent as a wart on the finger, it causes an immense deal of mental perturbation.

(4) *Ignorance due to the Perpetuation of Common Misconceptions.*—It is not always taught that the symptom-complex of rheumatism has not the same representatives in a child as in an adult, but that there are more frequently encountered, not arthritis, but cardiac dilatation, tonsillitis, chorea, emotionalism, nocturnal enuresis, and other nervous manifestations. A misconception of a similar character results in overlooking malignant disease of certain parts, because it is said never to occur in early life.

Another example is the popular identification of certain

substances in the motions of infants as food residues. These are really insoluble soaps, that is, mucus. Milk residues do at times appear in the stools; but, on the whole, it is a common mistake to suppose that fæces consist mainly of undigested and unabsorbed food, instead of merely disintegrated products of epithelium from the bowel.

(5) *Ignorance of recent important progress in Medical Knowledge.*—I do not think that a better example could be adduced than the evolution which has occurred in the knowledge and diagnosis of gastric diseases. Gastric ulcer used to be regarded as a common affection of young women, and the ratio of man to woman was given as 1 : 9. It is now evident that a large number of cases of appendicular gastralgia were diagnosed as gastric ulcer, and the sexual ratio of true ulcer has actually fallen to 1 : 1·25. Such an error arose from failure to utilize certain methods of diagnosis. Would any practitioner prescribe spectacles after merely listening to a patient's recital of symptoms? Yet, generally speaking, he will be prepared to treat his "dyspepsia," when he does not know if there is too much acid secreted or too little, whether the activity of the glands is satisfactory or impaired, and if the motility of the stomach is efficient.

b. MISTAKES DUE TO ERRORS OF JUDGEMENT.

The distinction of errors due to inexperience from those which may be attributed to ignorance is in reality artificial, but I want to err on the side of multiplying headings rather than otherwise. No case, for example, ever corresponds to a text-book description, which is a composite picture, as it were, of everything that is prominent, and only experience can teach what may be regarded as a sufficient sign of a certain condition. Want of experience applies particularly in chest cases, for there is the difficulty of setting a standard of sounds which are healthy, and it is quite a common enough thing to be in doubt which is the healthy and which the diseased side.

Indeed, it requires no little degree of experience to recognize what may be called normal. "Show me normal on the plate," was a favourite saying of Mr. Lockwood's, and the greater one's experience the more one appreciates the

wisdom of this criticism.

The poor victim who has sacrificed a normal inferior turbinate, which had been diagnosed as a nasal polypus, would sympathize with the importance of his medical adviser being able to recognize normal structures when he sees them. Many cases of functional albuminuria are treated as being of grave significance; creatinin in urine has been regarded as sugar. A reduplicated first sound may be mistaken for a presystolic murmur, when it may be due only to excitement or deep inspiration. In fact, a great variety of murmurs for the most part cardio-respiratory in origin, may be heard at the apex in the absence of disease, and some considerable experience is needed of the limits of normal sounds.

The need for judgement is well exhibited in the diagnosis of pregnancy. Judgement of human nature, particularly feminine human nature, is not quickly and easily acquired, and mistakes are numerous, until the young doctor has learned that pregnancy can never be excluded on *à priori* grounds of spinsterhood, separation, widowhood, social position, nor the patient's assertion that it is impossible. To overlook or wrongly diagnose a pregnancy is *the* one mistake we must not make.

Scabies is frequently not suspected in a cleanly person, more especially since it is in such circumstances atypical.

An obstinate case of rheumatism localized to one joint is treated as tubercle.

A child who is merely deaf is condemned by the inexperienced as being mentally defective.

It is clear that this topic could be extended *ad infinitum;* there can be no limit to the acquisition of experience, so there can be no limit to the number of mistakes which may be perpetrated. It has frequently been remarked that the best physician is the man who has made every kind of mistake so that he can make no more. This is a pretty picture which disposes to encourage and at the same time to stimulate, but I doubt if it is more than specious. So complex is the human body, so numerous are the possible errors, and so prone is the human mind to perpetrate mistakes which arise out of its deficiencies and not from the inherent difficulties of the problem it encounters, that the prospect

of making all possible mistakes is as remote as the prospect of learning one's profession simply by the contemplation of errors.

Examples of mistakes due to inexperience can, therefore, be multiplied in every branch of medicine. The enormous value of experience is evident in the early diagnosis of grave conditions. The most inexperienced can diagnose a case of disseminated sclerosis, when all the classical signs and symptoms are so obvious that they could be perceived a long way off with a telescope. The man of experience will be led by trivial early signs, which are quite insignificant to the novice. Think of the degrees of experience when one comes to the special 'scopes, none of which are any good without an expert eye behind them. Even with the naked eye, often experience alone can decide between a goitre and a lymphatic gland; a sarcoma and an hypertrophied tonsil; a syphilide and an eruption of pityriasis rosea or lichen planus; a drug rash and a closely-simulating exanthem.

c. MISTAKES DUE TO OBSESSIONS.

With all respect, I venture to think there is not one member of our profession who is immune to this cause of error. None of us will need reminding of the gross obsessions for which many eminent physicians and surgeons are notorious, or, perhaps I should say, famous. With the best intentions, it often seems impossible to avoid concentrating one's attention upon a certain hypothesis and unconsciously distorting phenomena to agree with it, whilst blinding oneself to other conditions which might have caused revision of judgment. I remember watching a class of 14 general practitioners, most if not all of whom must have been experienced men, examining a case of swelling in the right iliac fossa. But, because the demonstrator had skilfully directed their attention to abdominal conditions, not one examined the spine. As a matter of fact, the swelling was actually a tuberculous abscess, the result of spinal caries; a condition with which every gentleman present must have been as familar as with an appendix abscess.

This topic might well serve as the basis of a complete clinical lecture. Take the syphilomaniac, for example, who sees everything under the ægis of the spirochæta pallida, the

protean manifestations of which give a specious explanation for practically every sign and symptom which a human being can manifest or manufacture.

I have already implied that the sin of obsession is no less frequent among the leaders of the profession. It is somewhat amusing to observe that the laity have learned to appreciate this possibility, and request that they may not be sent to such and such a specialist, since he is sure to diagnose that particular condition. The real specialist has a fine sense of relative values, and his general training prevents a marked obsession. The good dermatologist, for example, is one who understands the skin and all that is within it. But pitfalls are many for the specialist who tends to lose his sense of perspective, and who fails to consider his patient as a whole. For "a stuffy nose" may be only a local manifestion of myxœdema, "a dry throat" an accompaniment of diabetes, a "laryngeal spasm" an expression of locomotor ataxia.

d. MISTAKES FROM FAILURE TO THINK ANATOMICALLY.

The late Mr. Lockwood, who will always be gratefully remembered by his pupils as a remarkable clinical teacher, perpetually emphasized the importance of "thinking anatomically." Confronted with a case of dysphagia, one should think all the way down from the tongue itself; there may be, for example, an inflamed gland beneath the sterno-mastoid. Since we can all claim sufficient knowledge to do this, it is obviously the only way to include every possible cause. Yet how rarely we take this precaution, save in such obvious cases as urinary troubles, in which the mind instinctively traverses the whole urinary tract.

Omission to think anatomically results in overlooking all sorts of reflex phenomena, *e.g.*, otalgia from carious teeth, when no complaint of toothache has been made. Cough, hiccough, and syncopal attacks may all have an aural basis, and abdominal pain in a child, which has been diagnosed as "congested liver," may be due to spinal caries, or in an adult occurring after exertion is most frequently an expression of cardiac trouble.

e. MISTAKES FROM FAILURE TO THINK AT ALL.

As a special variety of the preceding, one may include a category with the particular condemnation that the mistake is due to not thinking at all. An excellent example was

afforded by a diagnosis of progressive muscular atrophy, when a cervical rib was present. Had the physician thought about the condition at all, he would have realized that a unilateral wasting of that nature could not have been due to a myelopathy but to a unilateral cause.

f. MISTAKES FROM A RELUCTANCE TO ACCEPT RESPONSIBILITY.

I include this, naturally a very small, group as a type of deliberate error. Many cases of simple laryngitis are sent up to hospital as diphtheria without any attempt at actual diagnosis, in case the more serious condition may be present.

g. MISTAKES FROM INCOMPLETE EXAMINATION.

The category of errors due to incomplete examination is far and away the largest of all. Nearly all avoidable blunders result from this cause. Although mistakes may be perpetrated through one or other of the reasons I have already enunciated, how many mistakes would be avoided, if we made a point of a complete examination from head to foot, including the use of the ophthalmoscope and investigation of the urine! This is a preposterous counsel of perfection, but do we not all err on the side of examining incompletely? A patient presented himself some weeks ago with diplopia. An ocular nerve was paralysed, and nothing more definite than rheumatic neuritis was thought of. It failed to yield to symptomatic treatment, and a subsequent more searching examination, which included testing all the cranial nerves, led to the discovery that the fifth nerve was also involved (the masseter muscle was rather weaker on that side), and the diagnosis of early bulbar paralysis was established.

What are the causes of insufficient examination? First of all, because there is no time, owing to extreme pressure of work, for more than what, as a photographer, I should term a snapshot diagnosis. Very little removed from this and more culpable is the diagnosis, which is made upon the patient's symptomatic description without examining the part. Beware of "rheumatism." Which of us has not, with a scalpel, let "rheumatism" out of a swelling? And under this convenient diagnosis have masqueraded sarcoma, osteomyelitis, popliteal aneurysm, and acute epiphysitis.

A complaint of pain in the chest or cough demands at least a cursory stethoscopic examination; for the overlooking of

some gross lesion, merely through failing to look for it, will never be pardoned.

It may sometimes be advanced as an excuse, that the patient objected to some special examination. If the patient cannot be convinced that an examination is necessary, the case had better be relinquished, for it is better to lose a patient than to lose a reputation. The procedure of treating first and examining afterwards may lead to the unfortunate necessity of having to treat not only the disease, but the effects of your own treatment.

The omission of fundamental precautions is a fruitful source of avoidable blunders. A preposterous instrument has, at times, been devised to enable the chest to be auscultated without the preliminary precaution of removing the patient's clothes. The sole advantage which appears to be derived from this device, is the freedom from the familiar aroma of disrobing out-patient humanity. On the other hand, a pair of leather braces can simulate an excellent pleural or pulmonary adventitious sound. Again, how can slight modifications of the breath sounds be heard through a coat, waistcoat, and shirt, three vests, and a chest protector? A little more condonable are the mistakes arising from failure to examine more than a small portion of the chest. I have seen early tubercle of the right apex diagnosed, because the note at this apex was flatter and the breath sounds were louder. But a pleural effusion at the left base had been overlooked, which had compressed the left lung and caused hyper-resonance of the left apex.

One could give innumerable examples of errors due solely to limiting the examination to a portion only of the body. As a commonly occurring example, one may cite the diagnosis of a specific fever from a rash, sore throat, and fever, when a complete examination of the patient would have revealed an incompletely healed sore on the penis and enlarged lymphatic glands.

The most elementary precautions are sometimes all that is needed for the avoidance of gross errors. It is unpardonable, for example, to omit a digital examination of the rectum when appropriate symptoms are present. In any case of injury to the eye, it is as well to ask to be shown the instrument which caused the injury; for example, the missing

prong of a fork suggests a search inside the eyeball. In a nasal case, the patient should be asked to show the handkerchief—the pathological flag as it has been called.

An enormous number of grave errors may result from simply neglecting to take the temperature. Think how pyrexia coupled with headache and general seediness suggests typhoid fever instead of some trivial disorder; how the same feature allied to a cough, weakness, malaise, and indigestion builds up a strong suspicion of phthisis; how the temperature aids in the diagnosis of that obscure condition, pain in the side—whether neuralgia, herpes, muscular rheumatism, splenic infarct, abscess of the chest-wall or pleurisy, may be present; whilst, finally, its association with abdominal pain labels the condition as serious, straightway demanding an order for bed and further searching examination.

The thermometer, too, shows that the cure of a condition, which has been satisfactorily diagnosed, is not proceeding in a normal manner: *e.g.*, in pneumonia, delayed resolution, the development of an empyema, or the incursion of the pneumococcus to the peritoneum, the joints, or meninges; or in rheumatic fever, the danger-signal of endocarditis. There may be instanced as well the leaking of a gastric ulcer, or the urgency of a complete routine examination in chronic Bright's disease, in which the normal course is apyrexial.

These considerations briefly sketch the possibilities of mistakes arising from incomplete examination, but it is instructive to elaborate just a little further why such incompleteness may arise. There is a tendency, to which I am afraid we who are comparatively recently taught are rather prone, to rely too exclusively upon laboratory methods as a lazy expedient to escape the laboriousness of clinical investigation. As a contrast, error may result from a failure to utilize modern resources, and even to employ laboratory methods at all.

Mistakes may arise from sheer inability to believe that a serious condition can ever be present. In some cases, this may be due to pure obsession, but in others there does appear to be some grounds for the supposition that in certain people there exists a temperamental contempt for organic disease. Take such an example as the following. A woman with marked anæmia was regarded by her doctor as suffering from the

toxæmia resulting from nephroptosis. Such so-called toxæmia *may* produce an anæmia, but hardly of the degree present on this occasion. A more inquisitive observer pointed out, in the first place, that this supposed right kidney had a sharp lower edge, and was in fact the liver. The spleen was enlarged as well, and a blood examination supplied the ultimate confirmation of a diagnosis of spleno-medullary leukæmia.

If one were required to classify doctors upon a single characteristic, it would not be far outside the mark to distinguish them as those who see in every patient some grave disease, a diagnosis which they will not relinquish before its absence has been proved up to the hilt; and those who will not concede the possibility of anything but a trivial disorder (imagination, neuropathy, and so on), until the patient has demonstrated a formidable array of terrifying signs and symptoms, which it is impossible to ignore. The ideal diagnostician lies, I suppose, between the two. I well remember that during my house-surgeoncy at St. Bartholomew's Hospital, my corresponding house physician and I answered pretty accurately to these types—I may be spared the ordeal of further identification—and we made a very excellent blend in diagnosis.

A particular source of error is the overlooking of the more serious of two simultaneous conditions. It is a good general principle to include all symptoms so far as possible under one cause, but the complete connection may not be evident, as in malignant disease of the upper end of the rectum giving rise to very few symptoms but by pressure on veins causing piles. The difficulty is markedly increased when the less serious condition, which is first observed and upon which attention is naturally centred, may have nothing whatever to do with the graver one. Take a case, which came under my notice, of chronic ear discharge which developed cerebral symptoms. Trephining was the obvious treatment; but nothing was found, and the patient died of what was shown at the autopsy to have been uræmia.

h. MISTAKES FROM INHERENT DIFFICULTIES IN THE CASE.

Finally, I should like to include, as a small class, the variety of mistakes which may be said to arise from causes external to the personality. With all the resources which modern methods of investigation supply, it must be recalled

that these have their limitations. Take X-rays for example, and, as a familiar instance of their utility, the fact that they have demonstrated that fracture of the scaphoid, which once was regarded as a pathological curiosity, is now recognized as a fairly common occurrence. Yet X-rays are not unequivocal; difficulties bristle on account of the angle at which a picture is taken. Again, shadows are only shadows; anybody might mistake a gall-stone for a stone in the right kidney, or a calcified gland for either. Circumstances alone may supply insuperable difficulties. Think of the handicap which a bad light and a dirty skin impose in the diagnosis of a specific fever rash.

There are literally, what, for want of a better term, I call, inherent difficulties in a case, which occasion mistakes that not even the most methodical examination or the most profound experience seems to obviate. Urinary cases, for example, appear to offer so many traps. In the abdomen again, many people cannot tell an organ by feeling it, and not a few when they *see* it; moreover, the extra-abdominal causes of severe abdominal pain are many.

In this connection, I would like to dissociate a special form of difficulty. Nervous cases are said to be difficult. But are they not in reality merely complex, that is, made up of simple things? A nerve lesion must inevitably produce a certain chain of symptoms, there is not even a difference of opinion as to interpretation. I will give, as an example, the elucidation by a skilled neurologist, by the application of merely fundamental principles, of an apparently confusing list of symptoms. The patient, a woman of 40, complained of intense pain and tenderness in the right arm. She gave a history of pain down the left arm, and of a cerebral attack, accompanied by diplopia and left hemiplegia, four years previously. On examination, the right pupil was of the Argyll-Robertson type, and there was diplopia. On the right side, the knee jerk was absent; on the left side, it was exaggerated. There was no ataxia, no intention tremor, no ankle clonus, but a double extensor response was present. The Wassermann reaction was positive in the blood.

First of all, as regards the pain. Is this simply a lightning pain of tabes? No, because hyperæsthesia is not to be

expected. But syphilitic pachymeningitis in the cervical region would cause exquisite pain and tenderness.

Now to go back to the symptoms of four years ago. A lesion in the pons in the region of the crus, for example, gumma or thrombosis, especially the latter, would cause crossed paralysis. But this will not account for an Argyll-Robertson pupil and absent knee jerk on one side; hence, there is tabes as well.

There is, however, a knee jerk present on the other side. The obvious explanation of this is that tabes is only just beginning, and that one knee jerk has disappeared before the other. But, unfortunately, the left knee jerk is not only present but exaggerated. This is really because there is the combination of a hemiplegia and a tabes, and the hemiplegia explains the extensor response as well.

One feature alone is left for explanation—the extensor response on the right side. This is because the pyramidal tract on the non-hemiplegic side is not actually intact, but is affected on account of the existence of homo-lateral fibres.

So that the diagnosis is—

Pachymeningitis.
Specific endarteritis with thrombosis.
And developing tabes.

CONCLUSION.

In the contemplation of our successes we are naturally most pleased to indulge, but it is more instructive, if less edifying, to travel again the path of some past error. We are told by the poet that others' folly teaches not. Everybody makes some gross error in the course of his experience, and happy is he who makes it on some relatively unimportant occasion; happier still, if the only result is a determination never to make it again.

The cynical philosopher laments the pity, that in life we only get our lessons when they are of no use to us. It is worth while, nevertheless, to keep burning brightly that purifying fire, the fear of making a mistake, remembering in all humility that most mistakes were in reality avoidable, avoidable simply by method, the harness without which only the horses of genius can travel.

RADIOLOGY AND ELECTRO-THERAPEUTICS IN WAR-TIME.

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THE twin applied sciences of radiology and electro-therapy (including electro-diagnosis and prognosis) have, at the present time, assumed an importance hardly exceeded by that of surgery itself. Many of the operations now daily performed, as a result of bullet and shell injuries, could scarcely be undertaken without the help of the radiographer ; while the art of electrical nerve testing, though more limited in its range of application, is often the sole guide for the necessity or otherwise of surgical interference in cases of paralysis following wounds.

The work of the electrical department of a large military hospital at home is not, however, concerned solely with injuries received in the fighting line. The particular hospital to which I am attached serves a garrison of between one and two hundred thousand men. It is of interest to note the kind of cases with which they furnish the radiologist.

One might think—I certainly expected—that accidents in connection with riding would be numerous. When one considers that large numbers of men, who have never had any experience of horses, are being taught—at high pressure—to learn everything connected with them, many and severe injuries might be looked for with confidence. Such injuries do not exceed two or three in a month, and are rarely serious. This seems to me a remarkable fact, and says much both for the skill of the instructors and the aptitude of the pupils. The cynic might aver that the immunity enjoyed spoke rather for the cow-like nature of the mounts ; but I can testify, from personal observation, that the horses display quite an average amount of spirit.

Football, on the contrary, is responsible for putting a considerable number of men out of action, often for weeks, and

sometimes for months. Fractures of the tibia by direct, and of the fibula by indirect, violence are the most common injuries. Often the fractures take the form of cracks without any displacement, and cannot be diagnosed with certainty, except by X-ray plates. Sometimes the injury shows in one view only, *e.g.*, in a lateral but not in an antero-posterior. Cases are often sent in by the medical officers of regiments with a request to "screen." It cannot be too strongly urged that a mere screen examination is almost valueless in such cases. A negative result simply means that there is no gross displacement, and even the appearance of a definite fracture leaves one uncertain as to whether the whole extent of the damage has been ascertained. The prevalence of football injuries shows that the game must be played extensively among the troops at present in training. Obviously, the playing can take place only during the brief intervals between exhausting drills and marches; so that, as the lack of riding accidents speaks for skill, so does the plenitude of football injuries betoken, what I may term, extraordinary "resiliency."

A considerable number of cases are sent for examination for calculus of the kidney and bladder. The number of stones actually found is small in proportion to the number suspected; but the interesting point is, that hard marches and exposure seem to bring on symptoms suggestive of calculus in many men, who had previously believed themselves in good health.

There is a humorous side to this question of "stone and gravel." Men have been known to bring specimens of their urine to the bacteriological department, which undoubtedly contained "gravel" in large quantities; but the bacteriologist has reported that the deposit was of an "alluvial" nature! Malingering, however, has never been very serious in the new armies, and it tends to grow less and less. All who have "stuck it" so far must be pretty tough, both physically and mentally, and are unlikely to wish to escape after the most uninteresting part of their work is over.

In addition to the above, practically any diagnostic procedure which is carried out in a civil hospital may have to be undertaken. The assembling of men as soldiers in camps does not exempt them from the ordinary ills of life; though, as the newly raised forces consist of picked men, cases are

few in proportion to what obtains among an equal number of the civil population.

As to X-ray *treatment*, severe cases do not present themselves. Occasionally small patches of lupus are dealt with, and a few keloids and sluggish ulcers have been treated in the department. Unless there is a reasonable prospect of making a man fit for duty within a short time, he is invalided.

With the foregoing brief reference to the garrison side of the work, I pass to that concerned with the actual fighting. The radiography required is, in these cases, concerned wholly with the diagnosis of bone injuries, and the discovery and localization of bullets and shell fragments. On this subject I cannot hope to say anything which is new to the army surgeon, and shall, indeed, be lucky if I escape his criticisms; but the exigencies of the present war have thrust the problem of dealing with bullet and shell wounds upon hundreds of medical men, who have no previous experience in such matters. Numbers of auxiliary military hospitals are now scattered about the country, and to their medical officers I hope the following remarks may prove of some use.

When a case is brought in, the first question which arises is: Are any bullets or fragments of metal present? An "in and out" wound naturally suggests that nothing has lodged. But a bullet which, on the whole, escapes, may suffer some disintegration as it passes through the body, leaving irritating fragments behind. Serious damage to bones, too, may have occurred without complete fracture. Thus, a radiograph is desirable in all but the simplest of such cases. *Per contra*, the occurrence of only one wound affords no definite evidence that a bullet is present. A conical bullet may penetrate sufficiently to make an ugly wound, and yet drop out. Moreover, some men have undoubtedly had bullets extracted before being sent to England, but do not remember anything about the matter. If only one wound is to be found, and somewhere in its neighbourhood there is discovered a definite hard nodule which can be gripped between the fingers, it is probable, but by no means certain, that a piece of metal is present. Such cases have been operated on without success, and subsequent X-ray examination has proved the absence of any bullet or shell fragment.

There is another very important side to the question.

When there is only one wound, we are not entitled to give a negative report until we have taken X-ray plates of a considerable area of the body. It is not sufficient to screen. A bullet, quite obvious to radioscopy when its presence and whereabouts are known, may have previously escaped notice. Such extreme measures are, fortunately, not necessary in every case, for a bullet may travel to a distant part of the body and remain harmless. But any untoward symptoms, even if connected with an organ apparently remote from the original site of injury, should lead to the most rigid investigation. For instance, a bullet may enter the thigh, pass obliquely upwards, injure the bladder, and lodge in the opposite flank. In such a case, the bullet would not be seen even in a large plate of the region about the wound of entrance—and the vesical symptoms, if not severe, might be put down to some other cause.

The demonstration of a piece of metal in a radiograph, or on the screen, constitutes only the first step in the process of its localization. Surgeons inexperienced in this class of work are sometimes tempted to undertake the removal of a bullet on the strength of a single radiograph, because the shadow is in definite relationship with that of some familiar bony landmark. Only by great good luck can such attempts succeed. Usually, they end in dismal failure, for which the chagrined operator is sometimes illogically inclined to blame the radiologist—for whose advice he did *not* ask. A little thought will show that an X-ray plate deals only with two-dimensional space, whereas the surgeon has to work in space of three dimensions. A second radiograph at right angles to the first will help to some extent, but, unless a line, drawn vertically from the anticathode to the surface of the plate, happens to pass through the bullet, greater or less distortion must occur. These facts appear so elementary, that I feel I ought almost to apologize for venturing to expound them afresh. Experience proves, however, that they are by no means always fully appreciated by those who are being called on to do military surgery at the present time.

The ideal localization of a foreign body by means of surface markings necessitates the obtaining of four points on the skin, the lines joining which cross at right angles to each other and are perpendicular as well, or nearly so, to

the surfaces concerned. A simple and rapid method of obtaining such points, by means of a little instrument which I have called a "Ring-localizer," has been described by me elsewhere.[1] The method does not require the taking of plates, and, in the case of the limbs, head, neck, and parts of the trunk gives direct markings, without the necessity for any measurements. Elsewhere, as about the hips and pelvis, only the vertical line of the bullet can be ascertained directly. Some indirect method, involving triangulation and the displacement of images, must be used to find out the situation of the bullet on the vertical line.* But one must remember that a single mark on the skin, accompanied by the statement that the foreign body will be found so many inches below it, is not a sufficient guide for the surgeon. As an operation proceeds it often becomes difficult to say what was the original position of the localizing mark, and exact knowledge of the line of the bullet may be lost.

The first difficulty may be got over by drawing lines, at least four or five inches in length, at right angles to each other through the original mark (*i.e.*, on the surface through which the operation is going to be performed). These lines extend beyond the range of the "sagging" due to an ordinary incision; by using their extremities as a guide, two probes may be arranged across the wound, so that the site of the original localizing mark is indicated by their place of intersection. The actual line on which the bullet lies may be reproduced under all circumstances, provided that, by means of the ring-localizer, a mark has been made on the skin vertically *below* as well as directly above the bullet.

In our desire to localize quickly and easily by means of the screen only, we must not forget that plates are often necessary as well. The surgeon cannot have too many aids in his work. In the fleshy parts of a limb, screen localization gives all the information which the resources of radiology can usefully supply; but when the bullet is in close relationship with bone, photographs should always be taken when time

* My own preference is for a "life-sized" mechanical diagram with adjustable parts, which enables me to obtain a reading of depth without mathematical calculations. Such an instrument is made to my designs by Messrs. W. Watson and Sons, 194, Great Portland Street, W. They also manufacture the "Ring-localizer" above referred to.

permits. They should be taken with the tube and patient in the same relative positions as those in which localizing is done. The bullet image on the plate will then correspond exactly with the mark on the skin, and, by fitting the one over the other, the correct relationship of all the parts will be seen.

In places which readily admit of plates being obtained at right angles to one another, the antero-posterior and lateral views are generally to be preferred to a stereoscopic pair; but in the hips, shoulders, and parts of the spine, stereoscopy is often invaluable. Recently, I saw a man who had a rifle bullet in his face, one side of which was immensely swollen. It was easy to see that the bullet was lying in the neighbourhood of the antrum of Highmore; but antero-posterior and lateral plates failed to enable one to say whether it was or was not actually within the cavity. Stereoscopic plates were made, but in the first pair, which were of only average quality, it was not possible to make out the finest detail. A second pair enabled one to see that a thin plate of bone lay between the bullet and the observer. I gave it as my opinion that the bullet lay within the antrum, and this proved to be the case. So far as I know, stereoscopy is the only method by which the information desired by the surgeon could have been obtained.

Leaving radiology, I come to electro-therapeutics. Electrical procedures are of service to the wounded and disabled in the following ways: We can determine the gravity or otherwise of injuries to nerves and muscles; bring about the softening and absorption of fibrous adhesions; hasten the recovery of paralysed limbs; and finally, by the employment of high frequency, radiant heat, etc., to combat the effects of undue exposure, when it has resulted in rheumatism, neuritis, or a general breakdown of the bodily process.

We are fortunate in possessing a "Lewis Jones condenser set"[2] (made by L. Miller) for nerve and muscle testing. In this apparatus, 12 condensers are arranged in series, and are connected with as many studs, in such a way that discharges varying between $\frac{1}{2000}$ and $\frac{1}{40}$ of a second may be obtained. Muscles responding only to the longest discharges are in a state of degeneration. No electrical method of testing

will tell us if a nerve is mechanically divided. But if, six weeks after an injury, all the muscles supplied by a given nerve are found to require a No. 12 stud to excite them, and sensation is also abolished, the practice here is to operate. So far, in such cases the nerve has proved either to be choked by fibrous tissue, or actually severed.

When some muscles are less affected than others, and some sensation remains, it is impossible to come to any conclusion, until after several examinations extending over two or three months. If, for example, a muscle reacts at first to No. 9, and a month later to 8 or 7, spontaneous and fairly rapid recovery is likely to occur. But if the figures are 10 or 11, it may be assumed that certain nerve fibres, distal to the lesion, have died; so that, whether operation is done or not, one may predict with confidence that recovery of function will be at best a lengthy business.

In many cases, there is doubt as to the organic nature of the paralysis. Numerous cases occur to which, in ordinary civil practice, the term "hysterical" would be applied. Many of the patients are, however, men who have proved their bravery in the field, and it seems to me that "psychical" is a fairer term to use. The frightful sights and sounds of a battle-field, combined with some amount of actual personal injury, undoubtedly inflict at times a psychical trauma, which in all probability could be shown to have a definite physical basis, had we means fine enough to investigate it. Nothing could be further from the truth than to suggest any trace of malingering in such cases, yet it is undoubtedly true that in many instances the paralysis would vanish under sufficient mental stimulus—such as the classical "house on fire." The muscles in patients of this type are found to react to the slightest condenser discharges. On the other hand, many cases which still respond well to faradism, require 5 or 6 on the condenser scale before they will react, thus showing that some amount of organic change has occurred. Under the old system of faradic and galvanic testing, it would be impossible to separate such cases from the purely psychical type.

The condenser testing set is a great boon in a military hospital at the present time, and one feels that one owes a

debt of gratitude to Dr. Lewis Jones for having provided us with an instrument of such accuracy and simplicity.

As for treatment, we have time, under present circumstances only for those cases which are likely to show rapid improvement. No case is undertaken in which the muscles respond only to the longer condenser discharges, unless it has been shown that, although severe, the paralysis is spontaneously lessening. It is useless for the purposes of the present war to spend many many hours in freeing a limb from adhesions by chlorine ionization, when the power to work it will almost certainly be lacking for months or even years. In nearly all these cases, electrical treatment of some sort ought certainly to be given a prolonged trial, but a military hospital, where the outcry is always for more beds for the wounded, is not the place to do it in.

When, however, the nerve lesion is only of moderate severity, the results of ionization combined with faradization of affected muscles are little short of marvellous, and I have no hesitation in saying that electro-therapy, properly carried out, can return thousands of men to the front in a matter of weeks, who would otherwise have required months to recover.

From the purely military point of view, electro-therapy is only of value in so far as it can restore men to the firing line. From this standpoint, a man who can just manage to hobble a couple of miles at a time is no better than a helpless cripple. But to the individual concerned the difference is enormous; and, when it cannot wholly cure, electro-therapy will often give to the victims of war a measure of activity, such as they could not have hoped for before the advent of modern methods.

"Permanently unfit for service as the result of wounds." This is a hard saying, for the sufferers must often wait for skilled electrical treatment till the fighting is over. The qualified electro-therapeutist is busy with the more hopeful cases. There is a harvest ahead for quacks and charlatans, who will surely fatten on the pitiful wreckage of war.

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RECENT WORK IN RADIUM, X-RAY AND ELECTRO-THERAPEUTICS.

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RADIUM.

DURING the year, a considerable amount has been done to consolidate the knowledge gathered in the past few years, though no striking new use or new methods of usage have been discovered. The Radium Institute has published its second report,[1] confirming to a large extent the conclusions drawn from its first one. The report is highly important and very interesting, but, in my opinion, its results in one class of case falls singularly far below that of other radium workers, including myself; this is in rodent ulcer, in which, instead of getting about 95 per cent. of apparent cures, the Institute gets less than 50 per cent. Another criticism of this report which I would offer is, that in mentioning the amount of emanation sent out in applicators it reports their activity having been equal to 19 grams of radium bromide; that is to say, if they send out the equivalent of ½ gram of radium one day, and the same amount a week later for 38 successive weeks, they say they have sent out the equivalent of 19 grams. It would be just as reasonable for a person using a sealed-up radium salt, which has the same effects as the emanation, but is constant in quantity, to say that if he used 100 mg. every day for a year, he had used 36,500 mg. in a year.

As the literature in this country on the subject of radium is not very extensive, I have published a small volume on radium therapeutics, which was reviewed in THE PRACTITIONER (October, 1914).

Delano[2] gives a fairly accurate account of the uses of radium at the present day, according to various authorities. His articles would bear a lot of editing, and contain many

mistakes. For instance, he states that the β-rays are cut off by about 10 cm. of air, and a few lines later he says that it takes 1 cm. of *lead* to cut them off; as 1 cm. of lead corresponds to many metres of air, it is obvious that one of these statements is incorrect, and it is the former one. The average path of the β-particles in air is 250 cm., and the path of the most penetrating is considerably higher. Dominici finds himself in the quaint guise of Domenichi.

Simpson[3] records successful results with radium in the treatment of epithelioma of the lip, angioma, nævus pigmentosus, lupus vulgaris, syphilitic lesions, hypertrichosis, neurodermatitis (pruritus vulvæ), psoriasis, and lupus erythematosus.

Francis Williams[4] reports good results in the use of radium for the treatment of skin "cancers." Most of his cases are apparently rodent ulcer. He considers that the results show that the radium treatment of these cases is to be preferred to operation.

Renon, Degrais and Desbouis[5] obtain very good early results in the treatment of myeloid leukæmia with radium. Filtered rays from 30 to 33 cgm. are used, applied for 24 hours over a surface of 500 to 600 sq. cm. Relapse after 2 to 18 months is the rule, and at subsequent applications the radium has less effect. They suggest that these relapses may be due to faulty technique. Radium often succeeds where X-rays have failed.

Lazarus-Barlow has a good survey of the treatment of new growths by radiations in THE PRACTITIONER for March, 1914.

The Middlesex Hospital Reports[6] contain several articles of interest, ranging from studies of the influence of radium on cell-division and tumour-growth to snippy bits, such as observations on the absence of radium in healthy herrings. Lazarus-Barlow and Dunbar find that exposure of the muscle-nerve preparation of a frog to α-rays is accompanied by better maintenance of neuro-muscular irritability than in the control. These beneficial effects are exerted on the nerve and, to some extent, on the muscle, not on the nerve-endings. Lazarus-Barlow and Beckton find that if minute quantities of radium are allowed to act on the ova of *Ascaris megalocephala* in the resting stage, cellular division subsequently proceeds

at an accelerated rate. Greater quantities and more prolonged exposures retard the rate of division. α-, β- and γ-rays all produce this effect, but the α- appear to be much the most powerful. The quantities which produce the acceleration are, fortunately, millions of times smaller than those used in medical practice for local treatment. Mottram publishes an important investigation, from which he concludes that the action of the β- and γ-rays produces a disturbance in normal growth both in plants and animals, and that this disturbance is more marked if the cells be in a state of active division: the dividing ova of ascaris are at least eight times as vulnerable as the resting ova. The β and γ-rays are followed by profound changes affecting the chromatin. Russ and Chambers find that rat-sarcoma, exposed *in vitro* to a certain dose of β-rays, will not grow upon inoculation into normal rats; that sarcoma cells which have been irradiated may remain in the animal body for 60 days before giving evidence of a growth, and that the failure of the irradiated tissue to produce a tumour does not necessarily indicate their destruction at the time of inoculation.

Rowntree and Baetjer[7] have collected the various reports of the internal treatment by radium emanation. It is a curious fact that all these reports appear to come from Germany or Austria, so far as one can judge. The results are summarized in the following table:—

Disease.	No. of Cases.	Improved.
1. Chronic arthritis	411	371
Arthritis deformans	24	16
Muscular rheumatism	59	49
2. Gout	163	86
3. Neuralgia	59	47
4. Sciatica	115	91
Lumbago	5	4
Polyneuritis	8	8
Neuritis	5	2
5. Miscellaneous	186	163
	1,038	837

X-RAY THERAPEUTICS.

An important book by Kaye[8] has appeared during the year, dealing with the physical side of X-rays, which supplies a long-felt want, and should be in every radiographer's library. Although certain statements lead one to think that the author, at the time he wrote it, was not quite *au courant* with the most modern trend of radio-therapy, the book from the physical side is absolutely up-to-date.

An important event during the year has been the introduction of the Coolidge X-ray tube. This is on a principle entirely different from most X-ray tubes, though this principle had previously been utilized unsuccessfully by Lilienfeld. The tube is exhausted to a very much higher vacuum than the ordinary X-ray tube—so high that, if used in the ordinary way, no current will pass through it at all. The cathode, however, consists of a spiral of tungsten, which can be heated electrically by a current passed through it from an insulated accumulator; when this is raised to a white heat, it permits of the passage of high tension current through the tube, and the spiral then gives off a quantity of electrons, which are converted by the anticathode into X-rays. The amount of these electrons is dependent on the heat to which the spiral is raised. In order to focus the electrons on the anticathode, the spiral is placed to a greater or less depth within a molybdenum tube. The anticathode of this tube consists of a solid mass of tungsten, and the tube cools itself by radiation of heat from this, instead of there being a water-cooling or air-cooling arrangement. The tube is run with the anticathode white-hot if required, and it is claimed that, if not too sharply focussed, it will take 25 m.a. through a medium tube for an indefinite period. It is necessary to keep the glass walls of the tube cool in using these large currents by blowing air round the tube. I have now been using one of these tubes for some months, and it certainly has the advantage over the ordinary X-ray tubes that it is much more easy to keep the output of the tube constant, and it is possible to run a bigger current through it. The rays obtained do not seem to differ from those obtained by the older tubes. Coolidge claims that it produces homogeneous rays, but this has not been substantiated.

In experimental investigation, J. B. Murphy[9] found that

by irradiating rats over the whole body, he could make it possible to graft mouse-sarcoma on them, and keep it growing by transference to other irradiated rats. When the grafting was attempted on healthy rats, the graft always disappeared by the 9th day. In irradiated rats, he got persistance of the graft up to the 19th day. The explanation is, that the lymphoid tissue in a healthy rat causes failure of the graft, while in the irradiated rat the activity of this tissue is lessened.

Stevens[10] in an article on various forms of radio-therapy strongly urges the advisability of pre-operative radiation of malignant disease on the ground that it will probably prevent metastases from cells set free at the time of the operation. When one remembers that it has been proved that a properly irradiated tumour will not grow if transplanted (in mice), the advisability of this procedure becomes apparent. There is no necessity for any interval between the irradiation and the operation, for, though the results of the rays are not obvious at once, the effect on the cells is nevertheless immediate. He also advises post-operative treatment to prevent recurrence.

Pirie[11] describes perfectly rational methods for the treatment of hyperidrosis, hypertrichosis, acne vulgaris, rodent ulcer, and other conditions. He uses one Sabouraud dose, once a month for six months, for the first two conditions with excellent results, which, in the case of hyperidrosis, I can myself confirm. In rodent ulcer, he continues the treatment until from 6 to 12 treatments have been given after the ulcer has completely healed, or in other cases he uses one massive dose (four Sabouraud doses) and causes an acute burn which heals soundly.

One does not usually expect the writings of trade firms to be works of scientific interest, yet such a brochure, by W. E. Schall,[12] undoubtedly is. The catalogue of Messrs. Schall and Son has always been regarded as a high-class production for its information on X-ray and electrical apparatus, and this pamphlet of the junior partner is no exception. It contains a succinct and clear account of our methods of measurement of dosage and of the use of X-rays in deep therapy, and gives a useful comparison of the different qualimeters and quanti-

meters in use. This article is incorporated in the latest catalogue issued by the same firm, with much other matter of use to the beginner in electro- and radio-therapeutics.

X-RAY DIAGNOSIS.

A large quantity of literature has appeared during the year, especially in America, on the examination of the intestines with bismuth or barium salts. This must not be taken as indicating that radiographers are neglecting other branches, for it is undoubted that one's knowledge of many conditions has improved; as an instance, one may mention the radiographic examination of the lungs. Nothing, however, produces such theatrical effects as a bismuth meal, the black and white shadows appealing to the inexperienced far more readily, than the fine half tones of a chest radiogram.

Cannon[13] gives a historical account of the use of X-rays in the study of the alimentary canal, describing in some detail his own experiments, in conjunction first with Moser, and then with Francis Williams.

A. C. Crump[14] mentions a new method for the examination of the œsophagus. He introduces a bag of sausage skin or gold-beater's skin, which he then fills with bismuth mixture. He also gives a couple of tablespoonfuls of the bismuth mixture to swallow outside the bag. The advantage claimed for the method is that it outlines the whole œsophagus. The method will not secure adoption, for the following reasons:—

(1) A thick paste of bismuth and water outlines both the growth and œsophagus without the use of any such bag.

(2) It would be quite impossible for many patients with stricture to swallow two tablespoonfuls of mixture even without that in the bag.

(3) It is doubtful if the bag would go through a really tight stricture.

(4) The extraction of the bag is a very unpleasant process.

Tousey,[15] communicates a pessimistic paper, in which he issues warnings against X-ray screen examinations, and even against taking multiple radiograms. Tousey was unfortunately one of the early workers who suffered severely

from the rays, and to such a man, it is true, fluoroscopic examinations are a source of danger, but to an uninjured worker, using properly protected apparatus and properly protecting himself, there is no danger whatever. As for taking multiple radiograms, it is obvious that there is a limit, as well as to fluoroscopy, from the *patient's* point of view. This danger can, to a large extent, be diminished by having the anticathode a long way from the nearest point on the patient's skin, a minimum of 15 inches being advisable. But one has often observed the fluoroscope used for unnecessarily long periods, and the tube left running after that was necessary had been observed. Had Tousey limited his warning to a denunciation of this practice, he would have been justified, but the more extended warning is not in accord with modern experience. He starves his patient for 36 hours before the examination, allowing no solid food and no milk, and then gives an ounce and a half of bismuth oxychloride in mashed potato and a glass of water. The rectum he examines with a bismuth and barium enema.

Friedenwald and Baetjer[16] find valuable assistance from X-rays in the diagnosis of ulcers of the stomach and duodenum. They rely on the functioning of the stomach and intestines; bismuth cannot be made to adhere to the ulcer. Gastric ulcer causes a tonic contraction of the pylorus, with consequent retention of gastric contents, and the lesion may produce a deformity of the stomach outline as well. On the other hand, duodenal ulcer causes a hypermotility not only of the duodenum, but of the stomach itself, but in this case the spastic condition of the pylorus is absent, and, consequently, there is a rapid emptying of the stomach, its contents being completely emptied in from 40 minutes to an hour. In gastric ulcer, there may be primary quick expulsion of the contents, then the spastic condition of the pylorus appears, and there is a retention varying from two to four hours. In duodenal ulcer, a vacant area may appear in some portion of the duodenum, which persists throughout the examination, and at times bismuth may be observed running along on either side of this area. This vacant spot is practically absent, when the case is complicated by adhesions. Care must be taken to distinguish duodenal

ulcer from hypochlorhydria, in which condition there is a patulous pylorus, so that the stomach contents flow through quickly and freely, but unaccompanied by the active peristaltic contractions of the stomach seen in the former condition. Nothing but the clinical finding will differentiate these two conditions absolutely. In gastric ulcer, the condition can be diagnosed in certain situations only, and there is a tendency in some situations to get an hour-glass contraction.

One of the most important points, brought out in this paper, is that it is possible by means of X-rays to determine the progress of a case of duodenal ulcer. After four or five weeks' rest and treatment, the X-ray picture is unaltered, and if treatment is discontinued, the symptoms recur, but after longer treatment, the hypermotility of the stomach, the rapid emptying, and the vacant space in the duodenum gradually disappear, indicating the healing of the ulcer.

Carman [17] takes a very different line. He maintains that the "radiologic diagnosis of duodenal ulcer, unless corroborated by clinical data, is in most instances a mere guess." Similar appearances may be seen with disease of the appendix or gall bladder. He uses both fluoroscopy and radiography in his examination, and protests that radiologists have gone from the one extreme of extraordinary and ignorant rashness to the other extreme of extraordinary and unnecessary caution. He prepares his patient with castor oil and enema before the examination, and describes his routine for the examination of a gastric and a colon case. For the former, he uses two bismuth meals of different composition, given at an interval of six hours; for the latter he uses a barium enema.

L. Gregory Cole [18] contributes a valuable paper on the diagnosis of gastric cancer by serial roentgenography. He takes at least 40 radiograms, at various intervals after a meal of barium and buttermilk, and often takes as many as 80. As the materials for such an examination are expensive, it is truly a method for millionaires. Admitting the advisability of the procedure, it is within the reach of few, and is a method that needs care, for the total dose of X-rays administered must approach the danger limit. The article is illustrated by good radiograms of various types of growth and ulcer. Cole relies on irregularities in the stomach outline, which do not disappear

with the peristaltic wave, localized diminution of peristalsis, alteration in the width of the pylorus or its lumen, alteration of the shape or position of the duodenal cap or of its position in relation to the lumen of the pylorus. Cole claims to have made a correct diagnosis in 91 out of 94 of his cases, that were subsequently operated on.

Case,[19] after reviewing the literature on antiperistalsis in the colon, which goes to show that from a point to the right of the middle of the normal transverse colon feeble anti-peristaltic waves pass to the cæcum, summarizes his conclusions as follows :—

"(1) I have seen in man the tonic constriction ring, in the transverse colon to the right of the middle line, described by Cannon and others in animals. From this tonic ring slowly moving anti-peristaltic waves have definitely been seen to pass rhythmically towards the cæcum.

"(2) Definite rapid anti-peristaltic movements, resembling in every respect but direction the mass movements described by Holzknecht, have been seen in the iliac and descending colon.

"(3) Following ileosigmoidostomy, retrograde peristalsis in the colon has been observed in every case examined, without exception.

"(4) Exaggerated anti-peristalsis may be regarded as a sign of serious bowel obstruction, and may be expected in spastic constipation and obstruction from benign or malignant processes. It is especially valuable as an accessory sign in carcinomatous obstruction in the bowel."

This anti-peristalsis is important in cases of fæcal fistula, for, if the ileum is transplanted too near to the fistula, the fistula will not close. Case further records some interesting observations on the other movements of the large bowel, including his observations on mass peristalsis. This paper should be read by everyone interested in abdominal diseases or abdominal skiagraphy.

He finds that, when tested with a bismuth enema, incompetence of the ileo-colic valve occurs in one case in six, and, in view of the anti-peristalsis in the proximal half of the large

bowel, this is of great importance. Subsequent examinations, up to as many as five, have always confirmed this incompetence when it existed. This ileo-colic insufficiency is associated with constipation, not with diarrhœa, and with ileal stasis, not hypermotility. He uses no aperients or other previous preparation of his patients.

In another article,[20] Case discusses the use of X-rays in the diagnosis of carcinoma of the colon. He examines both by the bismuth meal and the barium clysma, and in the latter urges that the technique of Haenisch should be followed to the very letter in order to obtain reliable results. In addition to dilatation of the colon on the proximal side of the lesion and to a demonstration of the obstruction itself, he claims attention to another sign of serious colon obstruction, namely *exaggerated* anti-peristalsis.

Jordan[21] gives a description of the mass-peristalsis movements of the large intestine. He has not himself observed anti-peristalsis, and does not consider Rieder's evidence in favour of this satisfactory. He was apparently unaware at the time his paper was written of the work of Case, Roith, Cannon, and Jacobi.

Quimby[22] has a paper on the X-ray examination of the appendix. He finds that 90 per cent. of his cases, in which the appendix has not been removed, give sufficient data to determine the position and condition of that organ—a higher percentage, it would seem, than most workers obtain. It fills in from 6 to 30 hours, as a rule. He uses manipulation of the cæcum in some cases to show the appendix.

Dennis[23] enters a plea for the more extensive use of X-rays to demonstrate the position and extent of fractures of the skull. While more use seems to be made of this method in this country than in Australia, there are still a large number of head injuries which are not radiographed, owing to the persistence of the superstition that a fracture of the skull cannot be shown. With a modern apparatus, there is no difficulty in showing such fractures.

Binny and Lund[24] report 18 cases of separation of the lower femoral epiphyses, and give skiagrams of some of them.

ELECTRO-THERAPEUTICS.

In electro-therapeutics, the feature of the year has been

a steady increase in the use of diathermic treatment, both for surgical and medical purposes, but especially the former. The electro-cardiogram too is coming into much more common use, and is becoming much better understood. Watson-Wemyss and Gunn [25] give a description of the method of making simultaneous electro- and phono-cardiograms.

A book of interest more to dentists than to electro-therapeutists has appeared from the pen of Sturridge,[26] whose work on ionic medication of the teeth is well known. The book starts from the beginning of the subject, and has a large section on physics, as well as one on radiography of the teeth. Sturridge finds zinc and copper ions an effective means for sterilizing septic roots, and he also uses ionization extensively in the treatment of pyorrhœa alveolaris. Other uses are found for the employment of ions in dentistry, for instance, the electrolytic bleaching of teeth.

The method, apparently introduced by Beer in 1911, of treating papilloma of the bladder by the endo-vesical application of the high-frequency current, is among the most successful ways of dealing with this disease when it is localized; either the high tension high-frequency from an Oudin resonator, or the low tension current of the diathermy machine may be employed. Gehrels,[27] who gives a good description of its use, employs the latter method, while in America the former is more in vogue. In either case, the principle is the destruction by heat of the tumour and sparking is avoided, the heat being obtained by concentrating a large current on a small platinum electrode insulated to its tip and passed by means of an operating cystoscope. The application causes little or no pain and is made once a week, after the destruction of the growth, periodic cystoscopy is used to detect any early recurrence.

Bugbee [28] uses the high-frequency spark to relieve vesical obstruction "from a hard fibrous prostatic ring, prostatic nodules after perineal operations, median bar obstructions, a small median lobe, and diffuse carcinoma of the prostate and vesical wall." He uses a small high-frequency coil, and applies the current by means of a long insulated steel wire passed through the cystoscope. A $\frac{1}{10}$th inch spark is used, and the tissue is destroyed for about $\frac{1}{4}$ inch below the surface. No

anæsthetic is required, and the treatment is applied in several sessions. Symptoms are much relieved or cured.

Geyser[20] recommends high-frequency currents in the treatment of tic douloureux, and claims satisfactory results in 80 per cent. of all cases. His explanation of the action is that vasomotor effects are produced.

In the latter part of the year, much attention has been devoted to the localization of bullets, pieces of shell, and other foreign bodies, and several improvements in our methods have occurred.

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NEW ASPECTS OF ECLAMPSIA AND ITS TREATMENT.

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Eclampsia is characterized by convulsions of the epileptiform type, occurring at or about the termination of gestation and dependent upon the pregnant state. In severe cases, there is usually a more or less marked amount of coma.

The disorder is invariably preceded by symptoms indicative of the retention of toxic materials in the body; but, unfortunately, these symptoms may be so slight, and may seem to be so unimportant, that they may be ignored or overlooked, and during this premonitory stage albuminuria may or may not be observed.

Eclampsia is not only a formidable and very fatal disease, but to-day its occurrence is nearly twice as frequent as it was a quarter of a century ago. It is, therefore, very natural that we should ask ourselves what changes in our mode of living have occurred during the last 25 years, which would account for the recent very marked increase in the frequency of this terrible disorder.

In New York City itself, the deaths registered from eclampsia in 1902 numbered only 97, but in 1912 they numbered 171. To-day, in England and Wales, out of every 2,000 confinements one woman dies and seven, roughly speaking, are the subjects of eclampsia, while, strange to say, in Scotland this ratio is nearly doubled.

In former days, when blood-letting was common, and was resorted to as a remedial measure for eclampsia, it has been computed that one in every three or four mothers suffering from this disease died; whereas now, when blood-letting is seldom thought of, the maternal death rate has fallen to one in seven, and the mortality in the case of children born under such untoward circumstances has likewise been greatly reduced. These announcements can hardly surprise us, for, as

we shall learn presently, the withdrawal of a greater or less amount of blood would tend only to aggravate, and never to mitigate, this disease.

With all our hygienic improvements, the only retrograde changes in our mode of living, which have taken place during the last quarter of a century, and which can possibly be held accountable for the enormous increase in the frequency of eclampsia, are those which, needlessly and heedlessly, have not only been permitted but even encouraged to be made in the case of some of our most important food-stuffs—changes which have reduced unduly the mineral content more especially of those food-stuffs. The question of the mineral hunger thus provoked has so far attracted too little attention.

It is well known that eclampsia may occur without albuminuria, and that in fatal cases the kidneys may display little or no sign of having undergone any pathological change; moreover, women suffering from multi-cystic disease of both kidneys may go through pregnancy and child-birth without showing any eclamptic symptoms at all.

Some authorities attribute eclampsia to renal insufficiency and, consequently, the retention of urinary elements in the blood. Others again have suggested that the derangement is due to the passage into the maternal blood of poisonous substances, generated in the placenta or begotten in the fœtus itself. After a very careful analysis of facts, however, I have come to the conclusion that the intoxication results from the intermediary and not from the end products of nitrogenous metabolism, and from the retention, primarily and more especially, of these intermediary products in the nerve and muscle cells, because there is an insufficiency of the requisite mineral substances circulating in the body of the mother to satisfy her own needs and those of her infant in utero.

The fœtus derives its nutriment and mineral substances, under ordinary circumstances, not from food materials which have been assimilated and incorporated with the maternal tissues, but from those which have been assimilated and rendered fit by the liver and lungs for the maternal circulation. The metabolic substances available for and utilized by the fœtus are, as a matter of fact, the same primary metabolic substances that are attracted and utilized by the tissues of

the mother herself. The avidity of the embryonic tissues, however, transcends greatly that of the adult tissues as a rule, and this is true more especially of such important elements as phosphorus and calcium. Consequently, if there be in the circulating blood of the mother an insufficiency of any of the mineral substances, which are necessary for the maintenance of life and for the adequate fulfilment of the processes of metabolism, the claims of the fœtus are paramount and demand to be satisfied if possible, even at the expense and to the detriment of the maternal organism.

For the due fulfilment of the phenomena of life and the processes of metabolism in animals we have abundant proof that mineral substances are indispensable, and that they are, moreover, of greatest value when they are present in, what we are accustomed to speak of as, the organic form. It is common knowledge that phosphorus is as essential to animal life as air or water, and that for cell activity it is equally as valuable as nitrogen. For the display of functional activity and for carrying on the chemical changes which condition metabolism, every living cell must have phosphorus. Apart, therefore, from the question of any of the other mineral substances, which are essential to life, the actively growing cells of the fœtus must and will strive to have an adequate supply of phosphorus, and, as the avidity of the embryonic cells exceeds greatly that of the maternal cells, the latter, during pregnancy, will, under untoward circumstances, suffer from phosphorus hunger. Now, the oxidation of proteid matter in the organism takes place in intimate union with the phosphorus in the living cell; if, therefore, from any cause the phosphorus content of the maternal tissues, especially the nervous and muscular, becomes unduly lowered, then the formation of urea is hampered, and the intermediary products of nitrogenous metabolism are not evolved as they should be, but accumulate in the nerve and muscle cells. Independently of the auto-intoxication which thus results, the relative ratios of the mineral substances in the maternal cells become so altered, that the normal nerve and muscular reactions and irritabilities are changed, and convulsions are readily induced.

The woman who becomes pregnant in this twentieth century is seriously handicapped from the outset, because the average diet of to-day is very deficient in phosphorus, and in

calcium as well, and a diet poor in calcium is responsible for nervous and other disorders. In the cereal grains there is, it is true, an abundant supply of phosphorus and calcium; but, during the last 25 years, the roller process of milling has supplanted the burr-stone method of grinding wheat into flour, with the result that the marketable flour of to-day, from which our bread-stuffs are made, contains little or no phosphorus and little or no lime. Quite recently, too, there has sprung up the very pernicious practice of polishing and coating rice; a practice which has deprived this food stuff of much of its phosphorus and of other bodies, too, which are indispensable to the maintenance of health in cases in which this cereal constitutes practically the sole diet. It is early days yet to speak deprecatingly of the use of pasteurized milk and of butter made from pasteurized milk; but heating milk to 140° F. or higher so alters the chemical character of the milk, that it becomes altogether a less wholesome commodity than in the raw state. Now, either the dietary of our forefathers contained too much phosphorus and too much lime, or the dietary of to-day contains too little of these all-important mineral substances. The latter is undoubtedly the justifiable conclusion, for different forms of mineral hunger are accountable for the increase of polyneuritis, appendicitis, duodenal ulcer, beri-beri, and many other diseases.

The corpuscular elements of the blood are extremely sensitive to osmotic changes; consequently, the total molecular concentration of the blood must not be lowered unduly. In eclamptic cases, therefore, with a retention of the intermediary products of metabolism in the various body cells and a heightened irritability of nerve and muscle tissue, we can readily understand how blood-letting would aggravate rather than mitigate the state of the patient.

To safeguard the pregnant woman against eclampsia, we should ensure that her dietary contains an abundant supply of the mineral substances essential to her well-being. If a woman during pregnancy complains persistently of lassitude and headache, the urine should be examined; but whether it is found to contain albumen or not, the mineral content of her diet should be supplemented. As soon as eclamptic convulsions develop, an attempt should be made forthwith to induce labour.

RECENT WORK ON NERVOUS AND MENTAL DISEASES.

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INFANTILE PARALYSIS.

INFANTILE Paralysis, otherwise known as acute poliomyelitis, is now considered to be a contagious disease, capable of being spread from person to person, and sometimes occurring in epidemics. The way in which contagion is conveyed from one to another is not yet certainly known, but there is strong evidence that it may be carried by healthy contacts, so that a patient who is attacked has not necessarily been in direct relationship with anyone who has had the disease. Attempts to obtain a culture of the specific organism have not hitherto met with definite success, but that it is due to some infective organism is quite plain from the facts (1) that it is contagious; (2) that it occurs in epidemics which are more prevalent in summer and autumn; and (3) that, experimentally, the disease has been transmitted to animals. The crippling effects, which an attack is apt to leave, make it most important that adequate treatment should as far as possible be carried out, and an important contribution to this subject has recently been made by Mr. Robert Jones in the Annual Oration to the Medical Society of London.[1]

In this address, Jones first lays stress on the fundamental importance of early treatment, and in those cases in which the onset is accompanied by pain, he finds that relief can best be obtained by rigid fixation of the spine and limbs. He is in general agreement with other authorities when he says that, during the acute and early convalescent stages, rest is an important factor, provided always that any erratic postural positions of limbs are avoided. After the stage of pain has passed, and when the inflammatory processes may be supposed

[1] *Brit. Med. Journ.*, May 30, 1914.

to have settled down, he advises that the paralysed muscles should be put in a position of relaxation, and gentle massage and active movements carried out, but only in such a way that no strain of the relaxed muscles takes place. For example, if the flexors of the ankle are being kept relaxed, the feet should not be allowed to get into the position of equinus during massage, and any active movements that are made should consist of flexion of the joint beyond, but never below, the right angle. Voluntary muscular actions should be encouraged as soon as possible, but at first there should be no movements of joints, since the muscles are not strong enough to act against such resistances. For instance, when the lower limb is fixed and the knee extended in order to relax the quadriceps extensor, the first sign of recovery will be a voluntary twitch of the muscles. The patient should be taught to repeat this movement, but on no account at this stage should an effort be made to flex the knee. It is recommended that the massage in the early stages should consist of light vibratory effleurage applied as if to the skin, avoiding any rough handling which would be likely to do damage to the muscles.

This author's view on the stage at which all hope of recovery of a paralysed muscle should be given up is important, for, natually, it is a question which often arises. The answer, he points out, depends largely upon the treatment that has been received, but particularly upon an accurate knowledge of whether the paralysed muscle is suffering from the effect of over-stretching, or whether the paralysis is due to complete destruction of the corresponding cells in the spinal cord.

For a long time Jones has drawn special attention to the retardation of recovery that takes place when paralysed muscles are over-stretched. He has shown that, even in healthy people, after a group of muscles has been moderately stretched for 24 hours, a functional paralysis may occur, which, however, quickly recovers when the muscles are again relaxed. The effects of stretching are of such importance that it has been found that cases of dropped wrist, due to infantile paralysis, are capable of recovery in certain circumstances even many years after the original lesion has taken place, provided the muscles are kept continually relaxed by dorsi-flexion of the wrist. Emphasis is laid upon the necessity of

considering cases of infantile paralysis from the point of view of the whole nerve muscle apparatus, and not directing attention only to the cells of the spinal cord. The factors that are likely to lead to the undue stretching of muscles are posture influenced by gravity, inefficiently opposed muscular action, and deflection of body weight All such deformities may become fixed by the antagonistic muscles eventually becoming shortened. Thus, in undertaking the treatment of such a case, if the deltoid is affected, the arm should be kept abducted; in the case of paralysis of the brachialis anticus and biceps, the elbow should be kept acutely flexed; in paralysis of the extensors of wrist and fingers, the wrist should be dorsiflexed; and similarly, if the peronei are affected, the foot should be kept everted, and inverted when the tibial muscles are at fault. In this way, the muscles are kept relaxed and are given the best chance of recovery.

The different operations, for example, tendon transplantation, nerve crossing, and fixation of joints are discussed; for the details of these the reader should refer to the original paper.

PHENOMENA ATTRIBUTABLE TO SPASM OF CEREBRAL VESSELS.

While there is considerable doubt among physiologists as to how the vessels of the brain are directly governed by vasomotor nerves, there is, clinically, a good deal of reason for believing that spasm of these vessels can take place, and under the above title Dr. William Russell has recently given a clinical lecture on this subject.[1] He considers that many symptoms can be accounted for by arterial spasm in localized areas of the brain, and, in support of his view that this condition is a possibility, he draws attention to the alterations in size, that may be observed in the retinal vessels. He supports the view that migraine may be caused by arterial spasm, and considers that the visual changes in this disorder are associated with alterations in the retinal vessels. He thinks, too, that the loss of memory for recent actions, which so frequently occurs in elderly people, can also be explained on the same hypothesis, and illustrates the effects by the case of old people who from time to time get restless and sleepless or noisy and active in the night, and yet in the morning have

[1] *Brit. Med. Journ.*, May 16, 1914.

no recollection of anything they have done. In the same way, periods of mental excitement and incoherence occur, all of which the author considers can be accounted for by constriction of the cerebral arteries. The most suitable remedies for such conditions are vaso-dilator drugs, and the author considers the number of patients of this kind who respond to this form of treatment quite remarkable. The two drugs which he mainly uses are phenacetin and erythrol-tetra-nitrate.

Another type of case, to which the author draws attention, is that characterized by a complaint of sleepiness, of entire want of energy, and of marked forgetfulness, due to grave disturbance of the circulation in certain areas of the brain. The author acknowledges that such symptoms may indicate more than mere anæmia of brain areas, and mean that certain areas have passed into the stage of softening; but he considers that the cutting off of the blood supply, on which the softening depends, may in the first place have depended upon local spasm of the vessels, and that the preliminary evanescent stages suggest that this is what occurs. Even when softening has occurred, additional evanescent symptoms may still be added to those which are permanent, such for instance as dazed feelings, and entire inability to attend to business. These additional symptoms may come and go, and therefore, they may possibly be explained by spasm and be relieved by appropriate treatment, although the permanent changes cannot be affected. The subject is an important one, and if vaso-motor dilators bring the relief which Dr. Russell finds they do, they should be given, regardless of the fact that there may be still a doubt as to the exact mechanism by which these cerebral symptoms may be produced.

INCISION OF THE CORD AS AN OPERATIVE PROCEDURE FOR FRACTURE DISLOCATION OF THE SPINE.

Alfred Reginald Allen[1] gives an account of some further researches he has made respecting the effects of blows to the spinal cord and of the results of incision of the cord substance as the means of relief. The intensity of the impact applied to the cord in animals was carefully measured, and the effects of a subsequent median longitudinal incision,

[1] *Journal of Nervous and Mental Diseases*, March, 1914.

made directly through the injured area of the cord, noted. Beneficial results obtained by this means were ascribed to the drainage of blood and serum, which thereby relieved pressure on the nerve fibres and removed as well that which might later have given rise to chemical irritation with possible destruction of nerve fibres.

Summarizing his previous observations, Allen points out that there are two main factors to be considered in impact of the spinal cord: (1) direct injury to the axis cylinders, and (2) exudation of serum and blood into the substance of the cord. Allen has now experimented further in this direction, and has recorded the changes that appear in the cord 15 minutes, one hour, four hours, and at still longer intervals, after an impact of known intensity has taken place. The most notable change in the cord after one hour as compared with that of 15 minutes is that the intra-medullary hæmorrhage assumes a much greater proportion, and there is in addition a deterioration in the staining characteristics of the anterior horn cells, which latter change is still further marked three hours after the impact. Two hours after the impact, the hæmorrhagic areas are very conspicuous, and there is a large amount of œdema of the white matter. After four hours, the axis cylinders of the white matter of the lateral and posterior columns are found to be swollen, but in the fifth and sixth hours no more new characteristic changes are observed. When a posterior median longitudinal section of the cord is made through the injured area two hours after the impact, there is a flow of blood from the damaged part through the incision, and Allen calls attention to the important fact, that histological examination shows that the substance of a cord treated in this way is better preserved than that of one in which no such operation has been performed.

The practical importance of these researches lies in the possibility of such an operation being useful in cases of fracture-dislocation of the spine, and brief notes of three cases in which the procedure was undertaken are given. In the first case, the cord was found to be darker than normal, and on making a median longitudinal incision a considerable discharge of blood took place. The area of anæsthesia became much less after the operation, but unfortunately the patient

died from the effects of an injury to his skull, which took place at the same time the spine was broken. The second case was that of a man who had been struck on the back, with a resulting lesion of the first thoracic segment of the cord. An operation was performed about seven hours after the injury, but after some temporary improvement bed-sores developed, and death finally occurred. The third case was one of fracture dislocation of the thoracic region of the spine in a youth of about 17. The operation was performed four hours after the injury, and when the cord was incised blood spurted out. It is now more than a year since this patient was operated on, and function, though not restored, is said to be improving. As Dr. Allen says, this work is still in the experimental stage, and further evidence will be necessary before it can be said that a median longitudinal incision in fracture-dislocation of the spine is likely to be beneficial. One of the points emphasized is, that if the method is to be effective, it seems necessary that the operation should be performed within a very few hours of the injury. In any case, the subject is very important, since the operations for fracture-dislocation of the spine, as at present carried out, cannot be said to be very successful, and it seems quite possible, that this want of success may, at any rate partially, be due to failure in relieving the pressure that has occurred from œdema and hæmorrhage within the cord substance itself. Incision of the cord has also been carried out in cases of intramedullary tumours, as mentioned in the following paragraph.

INCISION OF THE SPINAL CORD FOR INTRAMEDULLARY TUMOURS.

Elsberg has recently shown that a considerable amount of success may sometimes follow operations, even on intramedullary tumour, by means of a method of extrusion. After an incision is made down to the growth, the intramedullary pressure causes the tumour to be exuded slowly from the cord substance. He has operated upon eleven cases of intramedullary disease, in all of whom, of the patients who could be followed, there was a very decided, and in some almost complete, recovery.

PRIMARY SPLENOMEGALY OR SPLENIC ANÆMIA: A CRITICAL STUDY, WITH SPECIAL REFERENCE TO THE PATHOGENESIS.

By THOMAS J. HOLLINS, B.A., M.B., B.Ch.

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Osler defines this affection as "a disease, probably an intoxication of unknown nature, characterized by great chronicity, primary progressive enlargement of the spleen, which cannot be correlated with any known cause (primary splenomegaly), anæmia of a secondary type with leucopenia, a marked tendency to hæmorrhage, particularly from the stomach, and in many cases a terminal stage with cirrhosis of the liver and jaundice (Banti's disease)."

This definition gives us a good clinical picture of the disease, the chief characters of which are—

1. A course of extraordinary chronicity, with no tendency to spontaneous cure.
2. Progressive enlargement of the spleen, which cannot be correlated with any recognized cause.
3. Anæmia of a secondary type with low colour index.
4. Presence of leucopenia.
5. Tendency to periodic gastro-intestinal hæmorrhage and hæmorrhage (occasionally) from other mucous surfaces.
6. Cirrhosis of the liver and ascites (Banti's disease), as a terminal stage in some, but by no means all, cases.

The form of the chronic splenic anæmia, associated with the name of Banti, was first systematically described by Professor Banti of Florence in the year 1883, though his first observations on this disease were published in 1881. We find him again contributing, in 1894, to some French and German journals, further articles on this subject, which he describes as an affection characterized by splenomegaly, with cirrhosis of the liver and ascites. Since then all subsequent

writers have attached his name to this disease (Banti's disease).

The relation existing between Banti's disease and splenic anæmia must clearly be understood, for a good deal of confusion has existed in the past on this matter. Banti's disease and splenic anæmia are not synonymous terms, as some authorities seem to suggest; Banti's disease represents the terminal stage of splenic anæmia, and does not necessarily occur in all cases of splenic anæmia. That it does not occur in all cases, is clearly indicated by the fact that many recorded cases of splenic anæmia do not show the features of Banti's disease, even when extraordinarily prolonged.

Banti himself regarded splenic anæmia as the antecedent of "splenomegaly with cirrhosis" (*Semaine méd.*, 1894). This idea was later amplified by Osler, and is now almost universally accepted. He says: "The conditions separately described in the literature as primitive splenomegaly, splenic anæmia, splenomegalic cirrhosis of the liver, or Banti's disease, are stages of one and the same malady." According to this view, primary splenomegaly and splenomegaly with cirrhosis are regarded as the initial and terminal stages, respectively, of splenic anæmia.

There has not only been considerable confusion in the use of terms in the past, but statistics have been vitiated as well by the inclusion of other forms of splenomegaly, under the heading of chronic splenic anæmia. As Rolleston points out in THE PRACTITIONER, April, 1914, instances of this are Gaucher's disease and cases of splenic enlargement associated with acholuric jaundice. I shall allude to these again under diagnosis. When all these conditions are carefully excluded—I mean, conditions which resemble splenic anæmia—there is still found a fairly large residue of cases of chronic splenic enlargement, which come into the category of true chronic splenic anæmia.

PATHOGENESIS.

The most interesting question in connection with this rare affection is the pathogenesis of the disease, and to this question no sufficiently conclusive answer has been given to satisfy those who have made a special study of

the disease. I may claim, however, to have demonstrated experimentally by animal inoculation that the Bacillus coli communis is at least one causal microrganism in this affection, and probably the only one. This point I shall return to later.

Osler, in his definition, speaks of it as "an intoxication of unknown nature," and most writers are agreed that it is probably due to a chronic infective process or toxæmia, but the state of our knowledge is very vague and indefinite on the subject. "The cause of this disease is unknown; bacteriological examination of the organs, cultures, and animal inoculation have all proved negative:" so writes the contributor on this affection in Osler and McCrae's System. Another writer says "No results have been obtained by blood cultures, puncture of the splenic during life, or by cultures of the diseased splenic tissue, and post-mortem examination of the organ has revealed no causal microrganism."

In the *Lancet*, November 1, 1913, is described a spleen of Banti's disease, exhibited by Dr. A. G. Gibson, showing the presence of streptothrix. "The organ showed general fibrosis, the surface was greyish pink, and dotted throughout it were small areas of pigment. Microscopically, these areas showed about the splenic veins masses of black staining material, which consisted of segmenting threads. After careful examination, he thought that there was no doubt that these constituted a growth of streptothrix." He discovered these parasites in 5 out of 100 spleens which he examined.

Rolleston (THE PRACTITIONER, April, 1914) doubts if any practical conclusions can be drawn from the presence of the streptothrix in these cases as to its specificity in splenic anæmia, owing to the fact that it occurred under such widely differing conditions. The five cases above referred to consisted of tuberculosis of the lungs and liver, with enlargement of the spleen; syphilis with splenic enlargement; chronic mediastinopericarditis, with splenic enlargement (slight); chronic cardiac failure, in which the spleen was not enlarged; phthisis, with hepatic syphilis and a spleen twice its normal size.

Ledingham (*Allbutt's System*) lays stress on the possibility of a traumatic factor in the ætiology of this affection. He points out that "many cases which showed symptoms of

splenic anæmia, or Banti's disease, have presented a history of previous severe abdominal injury, and that thrombosis of the portal vein with consequent splenomegaly, anæmia, and moderate cirrhosis of the liver has been proved on several occasions to follow injury." That this is so is conclusively proved by the observations of many competent authorities. How far the injury is responsible for the subsequent train of symptoms, and how far it is merely a coincidence, is difficult to decide. At any rate, a history of previous injury in recorded cases seems to be exceedingly rare. Watkin's article (*International Clinics*, Vol. IV., 20th series, 1910) on "The Relation of Thrombophlebitis of the Portal and Splenic Veins to Splenic Anæmia and Banti's Disease," is interesting in this connection. He says in conclusion, after bringing forward a mass of pathological evidence from recorded cases and cases which he has personally seen, "it is clear that in man the complex of splenic anæmia and Banti's disease, as formulated by Osler, is, in certain cases if not in all, the result of an obstruction to the splenic and portal circulation, particularly the former, and that this obstruction is most commonly the result of an old thrombophlebitis of the portal and its radicles . . . until it has been definitely shown that the splenic anæmia, or Banti's complex, can exist without any evidence of obstruction of the portal or splenic vein, then my conclusion must hold that the complex is no disease entity." Later on, in this paper, I shall mention one case which Mr. Connell showed me at Sheffield, in which there was no change in the splenic or portal vein.

Banti's views on the pathogenesis of this affection are interesting, and have found favour with a large number of modern observers. He believed that in this affection the spleen is primarily responsible for the morbid phenomena for the following reasons:—1. Splenic enlargement always precedes the anæmia, while cirrhosis of the liver is a terminal phenomenon and occurs last of all. 2. The pathological changes which he discovered in the spleen, and to which he applies the term "fibro-adenic," were regarded by him as peculiar to the disease. 3. The curative nature of the operation of splenectomy seemed conclusively to prove that the enlarged spleen plays an important *rôle* in the causation of

this disease.

He further believed that the anæmia was due to toxic substances elaborated in the diseased spleen, and that these diseased substances later produced thickening of the splenic vein and cirrhosis of the liver. The histological changes in the spleen, which Banti regarded as peculiar to this disease, are by no means confined to splenic anæmia, but may occur as a result of a number of morbid conditions, so that they cannot be looked upon as in any way pathognomonic. Thus, Marchand found these changes present in a case, which he regarded as of a syphilitic origin (*Allbutt's System*).

The relation of the spleen to this affection has been the centre round which there has been much discussion. Since Banti first brought the disease prominently before the notice of the profession, the view most accepted now is that the spleen forms the headquarters of an extensive chronic intoxication, which has its origin in the gastro-intestinal tract, and that the products of this chronic infective process are conveyed to the spleen by the blood-stream. The anæmia is believed by some followers of Banti to be due to some toxic material manufactured in the diseased spleen; this, however, has never been verified. Sippy, experimenting with rabbits, injected intravenously 2 c.c. of splenic extract from a case of splenic anæmia. After 24 hours, the two rabbits he used for the experiment died, but this is not conclusive evidence of some "toxic substance" in the spleen as he argues.

The fact that splenectomy apparently cures this disease has been regarded as proving conclusively that the spleen is primarily responsible, and that there cannot be an active hæmic intoxication present; but this does not necessarily follow. We cannot conclude from the results of splenectomy that the spleen has been the centre of elaboration of some toxic substance, for the improvement resulting from splenectomy in cases of splenic anæmia may well be due—as some have suggested—to

1. Removal of a diseased and considerably enlarged organ which had been causing great mechanical inconvenience.
2. Setting up of an artificial collateral circulation.

Besides, the subsequent history of cases, in which splen-

ectomy has been done, is not sufficiently definite or of long enough standing to permit us definitely to state that this operation is curative. Three main theories have been advanced as to the relation of the spleen in the production of anæmia :—

1. *That the spleen gives rise to anæmia by increase of its function of hæmolysis.* One of the well-recognized functions of the spleen is hæmolysis. The increase in size of the organ in splenic anæmia suggests increase of this function, with a resultant drop in the number of the red corpuscles and well-marked anæmia. In the *Lancet*, Aug. 23, 1902, Barr advocates the view that the anæmia is due to vaso-motor paresis of the splanchnic area, and that this paresis springs from a diseased condition of the visceral sympathetic ganglia. This, he says, leads to great engorgement of the abdominal viscera, especially of the spleen and liver, increased hæmolysis resulting in oligo-chromæmia and oligo-cythæmia.

In 1911, Sutherland and Burghard (*Proc. Roy. Soc. Med.*) advocated the view that the affection is due to loss of vaso-motor control in the splenic artery, leading to congestion and hyperplasia of the spleen. This hyperplasia, they assume, leads to increase of the hæmolytic function of the gland. They suggest that the spleen in splenic anæmia resembles the enlarged thyroid in Graves's disease. Against this is the fact, that the enlargement in splenic anæmia is not a pure hyperplasia, but is due to a chronic fibrosis; in such a condition, we should expect the spleen to show diminution rather than increase of function.

2. *That the spleen is the centre of a chronic infective process.* This process, it is considered, has its starting point in the alimentary tract, though Banti did not hold this view, and the toxin is conveyed to the spleen by the blood-stream. Having established itself in the spleen, this toxic process produces anæmia by inhibition of blood-formation. Against this, however, is the fact, that it is extremely doubtful if the spleen has a hæmopoietic function in the adult.

3. *That the spleen acts mechanically in the production of anæmia.* Rolleston, whose views on the relation of the spleen to anæmia I have mainly followed, advances the following pathological explanation of the hæmorrhage and resulting anæmia :—" Torsion of the splenic vein would divert the venous

blood from the spleen into the vasa brevia, the normal blood-current being reversed, and cause great dilatation of these veins and so œsophageal varices, from which copious or occult bleeding might result."

This hypothesis satisfactorily explains the anæmia, but not the subsequent hepatic cirrhosis in the further stage of Banti's disease (THE PRACTITIONER, April, 1914). His conclusion on the matter is as follows :—"With our present state of knowledge, it seems most reasonable to believe (*a*) that in splenic anæmia a chronic infective or toxic process has its headquarters in the spleen, which, therefore, undergoes fibrotic enlargement; (*b*) that the large spleen mechanically causes gastric hæmorrhage, which is responsible for the anæmia; (*c*) that poisons conveyed from the spleen eventually induce cirrhosis of the liver."

These conclusions, however, are open to criticism. In the first place, cases of splenic anæmia without any apparent hæmorrhage are not unknown. I have such a case under my care at present, exhibiting all the well-marked characteristics of the disease—splenomegaly, anæmia with leucopenia—and yet there has never been any hæmorrhage. The anæmia, therefore, cannot be due in all cases to hæmorrhage. In the next place, if the spleen is the headquarters of a chronic infective process, one would expect that the toxic substance or substances elaborated there would be isolated; but repeated attempts have failed to discover any such toxic material, and injection experiments with extracts of the diseased spleen of splenic anæmia have revealed nothing. Sippy's experiments in this direction are, as I pointed out before, inconclusive.

Injection experiments with methylene blue seem to point to the conclusion that the blood from the spleen is distributed to the left lobe of the liver. Cirrhosis, however, is not confined to this lobe in splenic anæmia (Sérégé. *Journ. de Méd. de Bordeaux*, 1902, xxxii.). The only question that remains to be discussed is, whether this disease is due to an active hæmic infection or intoxication. Owing to the fact that the operation of splenectomy has caused immediate improvement in all the symptoms, the view that the disease is of hæmic origin has been strongly opposed. On the other hand, many authorities now hold the view that the relative importance of

the enlarged spleen in this affection is highly exaggerated, and that the conclusion drawn from the results of operation are erroneous.

My experimental inoculation of rabbits with the colon bacillus has led me to conclude that this affection is due to an active hæmic intoxication, and that the colon bacillus can cause all the features of this disease. Whether the colon bacillus is the sole cause, which is probable, or merely one amongst many causal microrganisms, future research will have to decide. The hypertrophy and fibrosis of the spleen and the anæmia are, I believe, due to an active intoxication by this microrganism.

It seems suggestive that, in from 50 to 80 per cent. of all cases of cirrhosis of the liver, splenomegaly is found, and proves, I believe, that the liver and spleen are attacked simultaneously by a toxic agent. Adami, who discovered the B. coli in the liver in cases of cirrhosis, is of opinion that this organism may be the cause of the cirrhosis. If this is so, "cirrhosis" may be more closely allied to splenic anæmia than is at present thought, in that they may have a common bacillæmic or toxic origin. The anæmia I believe to be hæmolytic, and due to a specific hæmolysin which, in the case of the bacillus coli, may be termed colilysin.

That the bacillus coli has a hæmolytic action on blood cells, I proved by experimenting with a culture in vitro. The microscopical evidence seems to disprove the idea that the anæmia is hæmolytic, for no deposits of pigment or broken-down cells have ever been discovered in the enlarged spleen, like those we get in the other hæmolytic anæmia such as pernicious anæmia On the other hand, in a chronic condition of this kind one would not expect to find evidence of active hæmolysis like that found in acute affections, for in many cases 20 or 30 years elapse between the recognition of the disease and the post-mortem examination of the enlarged spleen.

During the past five years, I have met with three cases of the disease, and have made a special study of it. In these cases, certain clinical facts arrested my attention, and led me to the conclusion that this affection is probably due to poisons absorbed from the gastro-intestinal tract, and that

these are most likely due to the colon bacillus. This presumption from clinical data has been substantiated fully by experiment. The clinical facts to which I refer are—

1. Two of my patients were females, and had a history of constipation.
2. Oral sepsis was present in one case.
3. The enormous numbers of colon bacilli present in the diarrhœic motions of one case of Banti's disease, which I met with in the stage preceding death.
4. In one case, nervous lesions, resembling those artificially produced by injection of animals with B. coli were present.
5. The evidence of other diseases associated with invasion by B. coli, especially coliuria.
6. The presence of B. coli in the normal spleen.
7. Cirrhosis of the liver is produced by toxins from the gastro-intestinal tract, and probably by the colon bacillus.

To discuss these points seriatim :—Recorded cases seem to prove that the male is more prone to this disease than the female. Statistics on this point, however, differ. Thus, the writer in Osler and McCrae's System says that the large majority of cases have been in males : 7 of his own 8 cases, 13 of Osler's 15 cases, and 19 of West's collection of 24 cases. On the other hand, of 16 cases reported in Great Britain, 5 were males and 11 females ; of a series of 50 cases of Banti's disease, described by Banti, 32 were females and 18 males. The Registrar-General has been good enough to inform me that 6 deaths from Banti's disease were reported in 1912, of which 3 were males and 3 females. In my own series of 3 cases 2 were females and 1 male. Statistics from different observers differ, therefore, with regard to the sex incidence. In my own cases, the proportion of females to males was as 2 to 1 ; this, with a history of marked constipation in two of them, led me to consider whether the bacillus coli might not be the causal factor, or one of the causal factors, in this rare disease.

The form of anæmia found in splenic anæmia is chlorosis, and Dr. Andrew Clarke is emphatic in stating that ordinary

chlorosis is the result of constipation, and that the constipation is really a copræmia due to the absorption of poisons from the large bowel. So emphatic is he on this point, that he alleges that if he could only use one drug in this affection, he would use a purgative (Osler, *Text-Book of Medicine*). What these "poisons absorbed from the large bowel" are has never been determined definitely, but my experiments, described below, make it reasonable to conclude that one at least of these poisons may be a specific toxin elaborated by the bacillus coli.

That oral sepsis and dental caries act as causal factors in anæmia has been ably demonstrated by Hunter, who has devoted his life to research work in this direction. The particular form of anæmia associated with oral sepsis, he terms "septic anæmia," and it is probable that it may act in one of two ways in producing anæmia:—

1. Directly, by causing toxæmia and subsequent anæmia.
2. Indirectly, by causing erosions and lesions of the gastro-intestinal mucosa which act as foci of infection.

In the diarrhœic motions of case No. 3, which I describe under Banti's disease, were found enormous numbers of colon bacilli. This case showed, too, a rise of temperature in the terminal stages and considerable frequency of micturition with much pain during the act, all of which seem to point to a generalized invasion by the bacillus coli.

Experiments on animals have demonstrated that intravenous injection of bacillus coli produces certain nerve lesions, *e.g.*, paralysis and sometimes atrophy of the muscles, especially in the posterior limbs. These symptoms are due to lesions in the cells in the anterior cornua of the spinal cord. These effects are noticed as well after inoculation with streptococci and staphylococci (Muir and Ritchie, *Bacteriology*). In Case No. 3, to which I have just alluded, there was marked wasting of the muscles of the extremities. It was particularly noticeable in the muscles of the thighs, and, to a less marked degree, in the pectoral and scapular muscles, as well as in the deltoids and muscles of the arm.

In the *Lancet*, August 23, 1902, Barr remarks on this wasting,

and attributes it to vasomotor paresis of the splanchnic area. This leads to retention of blood in the portal area, and consequently, to fall of general blood-pressure and diminished supply to the rest of the body. This view, I believe, is only partly correct; the more likely explanation is that the muscular wasting is due to the effects of toxins on the central nervous system.

That the bacillus coli occurs normally in the spleen seems to have been proved in a series of autopsies recently, when the organism was found present in all the spleens examined. It must be remembered, however, that this micro-organism migrates to distal organs with extreme rapidity after death. It is doubtful if any conclusions can be drawn from the presence of the bacillus coli normally in the spleen. Some are of opinion that, granted diminished vitality, the micro-organism may increase indefinitely here, and produce fibrosis and the subsequent changes associated with splenic anæmia. They compare its action to that of disease germs on the tonsil.

We know that when the "sentinel" action of the tonsil is in abeyance, germs may gain access to the system, and cause affections and inflammation in other organs, *e.g.*, acute rheumatism, endocarditis, etc. In the same way, it is quite reasonable to suppose that the colon bacillus, gaining a foothold in the spleen, may multiply, and, acting over long periods, destroy the blood-filter action of the spleen, and thus render possible the subsequent morbid changes of the disease. The relation of this organism to cirrhosis hepatis has been emphasized by Adami, who thinks it probable that it may be the cause of the affection. If so, the relation of ordinary cirrhosis to splenic anæmia may be closer than is thought at present. Removal of the spleen in cases of cirrhosis hepatis has been attended with general improvement, which seems to favour the theory of those who hold that cirrhosis may be largely splenic in origin (*Medical Annual*, 1914, p. 546).

The following is an account of my experiments. By the kind permission of Dr. Barwise, the county medical officer of health for Derby, and with the assistance of Dr. Thomson, the pathologist at the laboratories, Derby, who performed the

inoculations for me, I carried out the following experiments :—

Experiment I.—A rabbit weighing 6 lbs. was taken, and a careful count of his red cells was made ; the red cells were found to number 6,304,000 per cmm. The animal was then given, between the shoulders, a series of subcutaneous injections of a 24 hours' broth culture of B. coli communis. The first injection was given on May 30, 1914, and consisted of ·5 c.c. The animal showed no inflammatory reaction, exhibited no signs of constitutional distress, and its temperature remained normal (39°).

A second injection was given on June 4, consisting of 1·5 cc. The animal now showed signs of constitutional distress, and lost 3 oz. in weight in a few days. Owing to this, the third and last injection was not given until June 18, when 3 cc. of the culture were injected. On June 19, I killed the animal under an anæsthetic, having previously taken some blood from its ear. On making a blood count, it was now found that the red cells had dropped to 3,840,000, showing a reduction of roughly 45 per cent.

When the experimental animal was killed, another rabbit weighing 7 lbs. was killed at the same time and the spleens of the two animals compared. It was found that the spleen of the experimental animal showed an enormous increase in weight, being 2·935 grams, while the spleen of the normal animal registered only 1·904 grams, which may be taken as the normal weight of the rabbit's spleen, when kept in confinement.

To tabulate the results obtained thus far :—

	Experimental Animal before Inoculation with B. c.c.	Experimental Animal after Inoculation with B. c.c.	Normal Animal.	Net Result of Experiment.
	Per cmm.	Per cmm.	About	
No of red cells -	6,304,000	3,840,000	6,000,000	45 reduction.
	Grams.	Grams.	Grams.	
Weight of spleen -	About 1·900	2·035	1·904	54 increase.

Experiment II.—The next experiment I performed, with the object of finding out if this enormous reduction of red

cells was due to a hæmolytic toxin manufactured by the B. c.c. Half the spleen of the inoculated animal was taken (the other half being preserved and sections cut) and carefully macerated in normal sterile saline; the emulsion was then centrifugalized, and the supernatant fluid so obtained preserved. At the same time, the blood of the normal animal was taken, and the corpuscles washed in the following way. The blood was first defibrinated by shaking it up thoroughly with glass beads; then, equal parts of defibrinated blood and normal sterile saline solution were poured into the tube of the centrifugal machine and centrifugalized. When all the red cells had been precipitated to the bottom of the tube, the clear supernatant fluid was removed by means of a pipette. The tube was again filled up with fresh saline solution, the deposit was stirred up, and the resulting fluid again centrifugalized.

After this process had been repeated three times, the red cells were diluted with a sufficient quantity of sterile normal saline solution to bring the total volume up to the volume originally used. To the corpuscles thus washed was added some of the supernatant fluid from the macerated spleen :—

(*a*) A drop of each on a microscopic slide.

(*b*) In varying quantities in a series of test-tubes to find the exact percentage of hæmolytic power present.

On examining (*a*) under the microscope two hours later the red cells showed crenation, but no disintegration and no discharge of hæmoglobin had taken place. On examining again one week later, I was surprised to find that all the corpuscles had disappeared. This result was found in all the slides which I mounted (about half-a-dozen), while the slides containing the blood of the normal animal alone merely showed that the cells had clumped together and had run into rouleaux. This shows that the disappearance of the cells in the former case could not be due to artificial contamination, and indeed every precaution was taken to prevent this, sterile saline solution being used throughout.

The result of the test tube experiment (*b*) was negative. The tubes containing the splenic emulsion and washed cells were incubated for two hours at 37° C. Unfortunately, the tubes were not kept, for I feel certain that if they had been

incubated for two or three days, considerable hæmolysis would have been shown. I tabulate the details of this experiment :—

Splenic Emulsion.	Saline.	1 % Washed Rabbit's Corpuscles.	Result after 2 hours at 37° C.
1 cc.		1 cc.	No hæmolysis.
0·5 cc.	0·5 cc.	,,	,,
0·4 cc.	0·6 cc.	,,	,,
0·3 cc.	0·7 cc.	,,	,,
0·2 cc.	0·8 cc.	,,	,,
0·1 cc.	0·9 cc.	,,	,,

Experiment III.—The blood of the inoculated animal was placed in a jar, and allowed to stand for three hours, until a sufficient quantity of serum for experimental purposes had separated out. The supernatant fluid was removed, and centrifugalized to remove all corpuscular elements. The washed corpuscles of the normal animal were treated with the resulting serum in the same way as in the last experiment (*a*) on a microscopic slide ; (*b*) in a series of test-tubes.

The result in both cases was precisely the same as in the last experiment ; all the cells had disappeared after a week in the case of the microscopic slides.

The following table shows the result in the case of the test-tubes after 2 hours' incubation :—

Serum of Inoculated Animal.	Saline.	1 % Washed Rabbit's Corpuscles.	Result after 2 hours at 37° C.
1 cc.	—	1 cc.	No hæmolysis.
0·5 cc.	0·5 cc.	,,	,,
0·4 cc.	0·6 cc.	,,	,,
0·3 cc.	0·7 cc.	,,	,,
0·2 cc.	0·8 cc.	,,	,,
0·1 cc.	0·9 cc.	,,	,,

Equal parts splenic emulsion and equal parts serum of inoculated animal and washed corpuscles. } No hæmolysis.

In vitro Experiment IV.—The following experiment proves

that the B. coli has a solvent action on red cells. A culture of colon bacillus from an acid broth (80 cc. of decinormal oxalic acid per litre) was taken and incubated for 7 days at 37° C. Then it was added, as above, to washed corpuscles of human, ox, sheep, rabbit, and guinea pig. In the case of the rabbit's red cells, slight hæmolysis was shown; the effect on the others was negative.

The following table gives the results at a glance :—

BACILLUS COLI SOWN IN ACID BROTH, 80 CC. DECINORMAL OXALIC ACID PER LITRE; 7 DAYS' INCUBATION :—

Bacillus coli Quantities.	Human Red Cells.	Hæmolysis.	Ox Red Cells.	Hæmolysis.	Sheep Red Cells.	Hæmolysis.	Rabbit Red Cells.	Hæmolysis.	Guinea Pig Red Cells.	Hæmolysis.
cc. 1·0	cc. 1·0	None	cc. 1·0	None	cc. 1·0	None	cc. 1·0	Slight	cc. 1·0	None
0·5	,,	,,	,,	,,	,,	,,	,,	None	,,	,,
0·2	,,	,,	,,	,,	,,	,,	,,	,,	,,	,,
0·1	,,	,,	,,	,,	,,	,,	,,	,,	,,	,,
0·8	,,	,,	,,	,,	,,	,,	,,	,,	,,	,,
0·5	,,	,,	,,	,,	,,	,,	,,	,,	,,	,,
0·2	,,	,,	,,	,,	,,	,,	,,	,,	,,	,,
0·1	,,	,,	,,	,,	,,	,,	,,	,,	,,	,,

When I proposed to carry out this experiment, I did not know that Kayser had already demonstrated that the colon bacillus forms a hæmolytic substance (Besson, *Practical Bacteriology, Microbiology and Serum Therapy*). The following account of "colilysin" is given there:—"Colilysin is a powerful solvent of dog red cells; it has less action on horse, ox, rabbit, cells, and very little, and in some cases no, action at all on the red cells of other animals (man, guinea pig, birds, etc.). It may be kept at the ordinary temperature of the laboratory and is not destroyed by heating to 120° C. for half-an-hour. Some normal serums (those of man, horse, etc.) neutralize the hæmolytic property of colilysin, and an anticolilysin can readily be produced by inoculating various animals simultaneously with a 4 days' old broth culture of bacillus coli."

Experiment V.—Culture was made from the spleen of the

inoculated animal.

Result. Negative.

Experiment VI.—Culture was made from the spleen of the normal animal.

Result. Negative.

Experiment VII.—Culture was made from the blood of the inoculated animal.

Result. Negative.

Experiment VIII.—The normal and diseased spleen were embedded in paraffin, and sections (horizontal and transverse) cut and stained with eosin and hæmotoxylin.

Significance of these experiments.—To demonstrate absolutely that this disease is due to a hæmic infection and that the B. coli is the causal micro-organism in this intoxication, would require a series of inoculations through a number of animals. Inoculations with other bacilli, such as staphylococci and streptococci, would be necessary too; besides this, the effects of the other numerous intestinal bacilli must be determined experimentally before one would be justified in laying down an absolute conclusion that the bacillus coli is the sole cause of this affection.

On the other hand, the single line of experimentation which I followed, while not excluding the possibility that the toxins of other micro-organisms may take part in the causation of this affection, yet it does prove conclusively that the colon bacillus can produce a condition simulating splenic anæmia so closely as to be identical with it, and it proves that the bacillus can produce splenomegaly and anæmia, the two outstanding features of this affection.

The results of experiments 2 and 3 are exceedingly interesting. As mentioned above, the corpuscles, when examined two hours after mixing with the splenic emulsion and serum respectively of the inoculated animal, showed very little change, but when examined a week later they had all disappeared. What is the explanation of this strange phenomenon? It must be remembered, in the first place, that strict precautions were taken to prevent the possibility of artificial contamination, sterile saline being used throughout; in the second place, that the corpuscles of the normal animal mixed with the same saline solution were intact when examined

at the expiration of a week. The only feasible explanation is, that colilysin had developed in large amount in the interim, and destroyed all the red cells present.

This experiment, I believe, is the key to the explanation of the anæmia and blood changes of splenic anæmia and probably many other forms of anæmia that we have to deal with. To understand how this is so, we must follow the probable sequence of events that took place in the blood of the experimental animal after the inoculations. The first result of the injections with B. c.c. was the production of colilysin, which brought about the destruction of the red cells and consequent reduction in their number. Simultaneously, an antibody was formed, anticolilysin, so that when the serum of the experimental animal was used these two antagonistic bodies were present. When this serum was added to the normal corpuscles, the colilysin was probably not present in sufficient quantity to overcome the natural resisting power of the corpuscles, reinforced by the antagonism of the antibody anti-colilysin; consequently, no destruction of the blood cells took place immediately. Later on, however, owing to the absence of vital reaction, colilysin developed in large quantities, and the red cells were destroyed *en masse*. This is probably what takes place in man in splenic anæmia: the toxins of the B. c.c., are absorbed, and lead to the formation of colilysin and anticolilysin, which circulate in the blood; the anticolilysin normally restrains the destructive power of the colilysin, but the colilysin on the other hand gains the day when for any reason the vitality and natural resisting power of the individual are lowered. This theory has the merit of explaining the strange phenomenon noted by many observers, viz., that the blood count varies considerably in a case of splenic anæmia at different times, sometimes within so short a period as seven days. As mentioned above, the normal serum of man antagonizes the hæmolytic property of colilysin. This, however, is no serious objection to my contention that the bacillus coli produces the anæmia, for it is only reasonable to conclude that this micro-organism, acting over long periods, can break down the natural resisting power of the serum, and cause anæmia.

Two questions in connection with the subject of the

pathogenesis of this affection remain to be discussed, viz.:

1. Does the artificial production of splenomegaly with anæmia in the rabbit, by means of inoculation with the colon bacillus, simulate splenic anæmia as we find it in man?

2. Do the accepted facts, with reference to this micro-organism and its relation to disease, render it probable that the B. coli can produce a fibrotic condition of the spleen and subsequent anæmia, with, in some cases, gross morbid changes in the liver?

To both questions, I answer: Yes. I believe that the production of splenic anæmia in the rabbit, on the lines of my experiment, represents in an exaggerated way, but no less truly, what takes place in man over a long period with a relatively smaller dose of the micro-organism, and I believe an exactly analogous condition could be produced in animals by a series of minute inoculations extending over a long period.

With reference to the colon bacillus and its relation to disease, we know that the bacillus, which was first described by E. Scherick, is a normal inhabitant of the intestinal canal of man and animals, and that it has been isolated from all parts of the canal, even from the stomach; it increases in numbers from above downwards, and is exceedingly abundant in the rectum (Savage). It is to be found here normally, in company with a number of other micro-organisms (about 50 different species), both in health and disease. In the healthy individual, it causes no symptoms at all, and is usually non-virulent when isolated from the stools, but it may, and does, readily take on virulent characters.

Thus, experimentally, a very virulent strain may be obtained by suturing the anus of a guinea pig. The animal dies of intestinal obstruction, and the cloudy peritoneal exudate gives a pure culture of extremely virulent colon bacillus. In man, the same thing occurs under conditions associated with lowered resistance, diminished vitality, and particularly with chronic constipation, the virulence of the micro-organism being in-

creased in all these conditions.

The number of diseases for which this bacillus is directly responsible, or with which it is indirectly associated, is large, and its responsibility for the production of diseased conditions seems to be becoming more recognized. All observers are agreed that the bacillæmic conditions due to it are not, as a rule, serious, but may become sufficiently severe to point to a diagnosis of typhoid fever.

It has been isolated in the blood in some cases of septicæmia, and is the cause of some cases of enteritis, infantile diarrhœa, and choleraic diarrhœa. It is found in peritonitis following strangulated hernia, or perforation of the gut. From one case, I obtained a pure culture in an empyema following appendicitis. It may cause meningitis, endocarditis, pericarditis, broncho-pneumonia, and various affections of the biliary passages, such as suppurative cholangitis In many affections of the urinary passages, and in bacilluria, it is the causal germ, as well as in certain pelvic affections in women, such as salpingitis, oopharitis, and metritis. It is probably a source of anæmia in cases of chronic constipation. It has been isolated in the liver, where it presents various transformations, appearing sometimes as a diplococcus (Adami). This observer suggests that the liver has a bactericidal power on this bacillus and, possibly, on others absorbed from the intestine. He has found these polymorphic forms especially in cirrhosis, and suggests that the B. coli may take part in the causation of this disease (*Coats's Manual of Pathology*).

From what I have said, it is evident that, under suitable conditions, the colon bacillus may multiply enormously, and be converted into a virulent agent of disease, though normally it is innocent ; that it may light up various inflammatory conditions in the different organs of the body ; that a long continued intoxication by the products of this micro-organism may lead to a chronic fibrotic condition, which probably takes place in cirrhosis hepatis ; and that it produces a specific hæmolysis (colilysin), which, as I have demonstrated, may cause anæmia.

These accepted facts about the colon bacillus, especially when taken in conjunction with the results of inoculation,

point strongly to the conclusion that the colon bacillus may cause all the features of splenic anæmia, and may be responsible for the cirrhosis of the liver, which we find as a terminal stage in certain cases.

MORBID ANATOMY.

The spleen is greatly enlarged, but preserves faithfully its outline. It may weigh as much as 3 lbs., but does not attain the extraordinary size reached in cases of spleno-medullary leukæmia, or in Gaucher's disease (*see* below). Pathologically, it shows a general hyperplastic fibrosis, the sclerosis extending to the capsule, the reticulum of the pulp, and particularly to the Malpighian corpuscles. The pulp and Malpighian bodies are usually atrophied, often markedly so, and the fibrous Malpighian corpuscles show in many cases hyaline degeneration. The capsule usually shows signs of perisplenitis, and adhesions are mostly present, especially to the diaphragm. In one case, which Mr. Connell removed recently in Sheffield, I found no adhesions present, and there was no perisplenitis; the spleen weighed 11¼ ozs. The endothelial cells lining the pulp sinuses show various degrees of hyperplasia. Evidence of increased hæmolysis (broken down corpuscles and areas of pigment) is not found.

The microscopic picture of the spleen in this affection serves to distinguish it from the spleen in various other conditions of morbid enlargement. Thus in myeloid leukæmia, in which the spleen attains extraordinary dimensions, the microscopic picture is very distinctive. The organ in this condition is found to consist of tissue closely resembling marrow, masses of closely packed leucocytes take the place of the Malpighian corpuscles, which are hardly discernible. Among the cells are to be found macrophages, myelocytes, polynuclear leucocytes, and nucleated red cells.

In pernicious anæmia, the enlargement is rarely considerable; there is always evidence to be found of increased hæmolysis. The picture is one of sclerosis and of increase in the activity of the macrophages.

In Gaucher's disease, or primary endothelioma of the spleen, the characteristic feature present is nests or masses of long clear multinuclear cells, with occasional giant cells;

sometimes these cells fill the entire organ, and cause nodular elevations of its surface (Stengel). This condition, which has often been classified under the heading of splenic anæmia, for it presents all the clinical symptoms of that affection, has led to much discussion. Its chronicity—one case lasted 25 years (Osler and McCrae)—is a strong argument against the view, largely held, that it is a true neoplasm.

In Hodgkin's disease, the spleen is enlarged in about 75 per cent. of cases (Osler), but the enlarged spleen in this condition can readily be recognized, owing to the characteristic lymphoid infiltration.

Reports of autopsies seem to show that, even in the earlier stages of splenic anæmia, some degree of cirrhosis of the liver is present, although there may be no macroscopic evidence of this morbid condition. Thus, Banti admits that slight hyperplasia of the interlobular connective tissue does occur. There is as well fibrosis of the kidneys and pancreas (Ledingham), and this strengthens the idea that the disease is hæmic in origin.

The condition of the veins is of importance, owing to their relation to the hæmorrhage which occurs in this affection. The splenic vein is often enlarged and tortuous, because of the increased size of the organ and its liability to drag on its pedicle; endarteritis and patches of calcification may be found in it. In some cases, the vessel is reduced to the condition of a fibrous cord. In the spleen, which Mr. Connell showed me at Sheffield, there was no change whatever in the splenic vein, although the patient had suffered from repeated hæmorrhages.

The vasa brevia are dilated. The probable explanation of this change is "that they have at certain times to convey the blood from the spleen, a reversal of the normal current of the blood, when from twisting of the pedicle of the organ the splenic vein is temporarily occluded" (Rolleston, THE PRACTITIONER, April, 1914).

The veins at the lower end of the œsophagus are frequently found to be dilated and varicose, and ulceration may be present. Stenosis and calcification of the portal vein have been reported (Ledingham).

The lymphatic glands are normal, but Dock, Warthin, and Stengel found considerable enlargement of the hæmolymph

glands lying along the thoracic aorta and in the retroperitoneal area. They regarded this enlargement as compensatory (Ledingham). Various changes have been reported in the gastro-intestinal tract, such as generalized atrophy of the intestinal mucosa and thickening of the intestinal wall. Hedenius observed, in one of his cases, great localized thickening at the ileo-cæcal junction; he found the ileo-cæcal valve greatly narrowed, and the mesentery much thickened.

I append a table showing the weight of spleens in various pathological conditions, which I saw at the Victoria University, Manchester, by the kind permission of Professor Boycott.

Disease.	Weight of Spleen.	Condition of Splenic Vein.
	Ozs.	
Spleno-med. leucocythæmia -	47	No change recorded.
„ „ leukæmia - -	150	„ „
Leucocythæmia - - -	70	„ „
Spleno-medullary leucocythæmia	101	„ „
„ „ „ -	47	„ „
Hodgkin's disease - - -	18	„ „
„ „ - - -	28	„ „
Anæmic infarct - - -	15	„ „
Acute hyperæmic infarct - -	23	„ „
Fibroid enlargement - -	11	„ „
Secondary endothelioma - -	8	„ „
Malaria - - - - -	32	„ „
Hypertrophic cirrhosis (biliary) of liver.	50	„ „

The following details refer to three spleens excised in cases of splenic anæmia. Two of them are in the Museum at St. Bartholomew's Hospital, and the details were kindly furnished by Professor Andrews, Curator of the Musuem. The other is a case of Mr. Connell's :—

Weight	Condition of Splenic Vein.	Condition of Splenic Artery.
11¼ oz. - -	Normal - - - - -	Normal.
22½ oz - -	Enlarged, no calcification -	Intima thickened.
Not recorded -	„ „ -	Normal?

CLINICAL PICTURE.

The clinical picture of this disease is distinctive and may be summed up briefly under the heading of its cardinal features, —splenomegaly, anæmia, hæmorrhages, and changes in the blood. As a rule, the case is well developed before being seen by the physician. The first thing complained of usually is a tumour on the left side, or the patient may not even seek advice until an attack of hæmatemesis or epistaxis comes on. In the early onset, cases are never seen, and if seen could not be recognized, for there is nothing distinctive, the condition being one of simple splenomegaly, the anæmia developing subsequently. The history and symptoms of two cases I have had under observation are given, because they represent the type of the disease commonly met with.

Case I.—A man, 73 years of age, when first seen, was complaining of extreme shortness of breath and extreme debility, to use his own words, "everything was a trouble to him." On examination, I found that he was markedly anæmic, and showed signs of emaciation. His spleen was considerably enlarged, and extended 2½ inches below the lower margin of the ribs, and well beyond the median line in front. As he was very thin, the enlarged organ could be felt distinctly under the hands while examining, the notches on the anterior border being distinctly noticeable. He had had no hæmorrhages (hæmatemesis or epistaxis), but said that at times his motion looked very dark-coloured, which, I have no doubt, meant that he had "occult bleeding" from his bowels periodically. His blood was found, on examination, to be deficient in red blood corpuscles and in leucocytes, and the colour index was low. The actual count was: red cells 3,225,000, leucocytes 6,000. A differential count was not done in the case of the leucocytes. There was a history of obstinate constipation, 10 days often elapsing before the bowels were relieved. This patient, after being under my care for about two months, eventually drifted out of my area, and died, I believe, of some intercurrent affection.

Case II.—This case I have under my care at present. She is 64 years of age, and I have attended her during the last 3½ years. With that unreasoning prejudice which we find among a certain class, she refuses all idea of hospital treatment, so that she is practically confined to the house. She has all the symptoms associated with chronic anæmia. Her spleen is greatly enlarged, reaching the middle line in front and almost 2 inches below the costal border. She gets periodic attacks of sharp pain in the splenic region, associated with vomiting and difficulty in micturating. She has had no hæmorrhages. There is a long history of constipation, and she has a septic mouth. The origin of these periodic attacks of pain is interesting. It is probably due to twisting or dragging of the pedicle by the enlarged spleen; the spleen is never tender on being grasped between the hands, and there has never been any perisplenitis. The vomiting and difficulty in micturating is also due probably

to pressure from the enlarged organ. Her blood count is remarkable for the exceedingly low number of whites. The actual count is red cells—3,640,000 per cmm. White cells 1,800 per cmm.

These two cases illustrate pretty clearly the type of the disease usually met with in practice, the only classical symptom absent being hæmorrhage, but in case I. there were indications from the history that "occult bleeding" had taken place from the bowel, although, during the two months of my attendance, no dark motions were passed. Case No. III., which I describe under Banti's disease, had frequent profuse hæmorrhage from the nose.

The splenic enlargement in this disease always precedes the anæmia, and sometimes it precedes it for long periods (Lyon), so that a case in its early stages represents merely a simple splenomegaly. The enlarged spleen often attains considerable dimensions, but is rarely as large as the spleen of myeloid leukæmia. It varies in size according to the stage of the disease, the more chronic the condition the larger the spleen. Thus in Case III., which was extremely progressive and rapidly fatal, the spleen enlarged progressively within a very short period. When first seen, it was merely palpable, 11 months later it extended 2½ inches below the umbilicus and over the mesial line in front to the extent of 2 inches. Its sharp edges and notches could be felt distinctly, its general contour was preserved, and it was found to be generally enlarged, smooth, and even.

The enlarged spleen is not usually tender on pressure, but in this case it was decidedly tender, and there were recurring attacks of perisplenitis, which were always associated with increase in the size of the organ (*see* below). In the other two cases, the enlarged organ was firm and smooth to the feel, and neither tenderness nor perisplenitis was present.

The following table shows the extent of splenic enlargement in my cases :—

Case.	Disease.	Middle Line.	Laterally.
I	Splenic anæmia -	¾ in. beyond - - -	2½ in. below costal border.
II	,, ,, -	Reaches middle line -	2 in. below costal border.
III	Banti's disease -	2 in. beyond and 2½ in. below umbilicus.	——

The anæmia is of the secondary type, with a low colour index, and is rarely very intense ; it varies, however, in intensity in the same patient at different times. Some writers think that too much stress has been laid on the anæmia, and regard the term splenic anæmia as a misnomer, or at any rate as being misleading. In the earlier steps of the disease, no anæmia, or at least nothing more than slight reduction of the hæmoglobin is present. At what stage in the disease anæmia first begins to make its appearance, we do not know ; what we do know is that sooner or later anæmia does appear, aggravated in most cases from time to time by periodic hæmorrhages from the gastro-intestinal tract or from the nose.

In many cases, the most careful observation by competent clinicians has failed to detect any bleeding at all, and in these cases the anæmia must obviously be due to a toxic factor, a specific hæmolysin (colilysis) manufactured by the colon bacillus, and possibly hæmolysins manufactured by other bacilli. To this I have referred above. After hæmorrhage, often very severe, we find that sooner or later there is a restoration to the normal condition before hæmorrhage. How this is brought about we cannot definitely say. It may be that the enlarged hæmo-lymph glands are responsible, or that the treatment which a patient undergoes after such a hæmorrhage (*e.g.*, rest in bed, internal medication, intestinal antiseptics, etc.) tends to improve his vitality, and increase his resistance, so that the possibility of further elaboration of toxins in the intestinal tract is diminished, with a consequent return to normal of the blood condition.

The most usual form of hæmorrhage in splenic anæmia seems to be hæmatemesis, and it is characterized by periodic recurrence extending as a rule over a long period of years. In some cases, it is very severe ; a pint or more may be lost at once. Its importance lies in the fact that it is the determining factor in deciding whether splenectomy is desirable or not. In a recent case, at Sheffield, in which Mr. Connell removed the enlarged spleen, the patient had been brought into hospital three times within 18 months with severe hæmatemesis. In some cases, on the other hand, there has been no evidence of gastro-intestinal hæmorrhage, as in the case which I have under my care now. It is probable, how-

ever, that in a large percentage of such cases hæmorrhage occurs periodically *per rectum*, which escapes the notice of the patient; this occult bleeding seemed to be present in one of my cases.

The hæmatemesis owes its origin to one of the following causes:

1. Congestion of the gastric mucosa.
2. Erosions and necrosis of the gastric mucosa, due to bacterial influence.
3. Ulceration and rupture of dilated veins at the lower end of œsophagus.

The congestion of the gastric mucosa and the piles at the lower end of the œsophagus are brought about by the mechanical effects of the enlarged spleen, which cause occasional torsion of the splenic vein, a reversal of the current of blood into the vasa brevia, and consequent engorgement of the gastric mucosa. This mechanical theory, advocated by Rolleston (THE PRACTITIONER, April, 1904), is clearly inadequate as an explanation of hæmatemesis in all cases.

1. If the hæmatemesis in this affection is due to torsion of the veins, we should expect to get hæmorrhages in other forms of splenic enlargement which would equally cause torsion of the veins.

2. In many cases, in which severe hæmatemesis has occurred, no changes are noticeable in the splenic vein after removing the organ or post mortem. As I mentioned, there were no changes in the vein in the case which Mr. Connell was good enough to show me recently in Sheffield, although there had been recurrent attacks of severe hæmatemesis. In such cases, erosions of the gastric mucosa due to the action of bacilli are probably responsible, forming it may be a large percentage of all cases.

In the later stages, other forms of hæmorrhage may occur. Thus, in case III., there were repeated attacks of severe epistaxis, occurring about three and four times daily. Other rare forms are oozing from the gums; retinal hæmorrhage, and hæmaturia. Petechiae sometimes occur.

The blood-picture in splenic anæmia has no distinctive

feature, and is not pathognomonic. Its main features are as follows :—

1. Reduction of red cells.
2. A more than proportionate reduction of hæmoglobin.
3. Leucopenia.
4. A relative lymphocytosis.

The following table shows the blood picture in my three cases.

Case.	Disease.	Per c.mm. Red Cells.	Per c.mm. White Cells.	Hæmoglobin.
I.	Splenic anæmia -	3,325,000	6,000	45 per cent.
II.	Splenic anæmia -	3,640,000	1,800	47 per cent.
III.	Banti's disease -	3,600,000	Record lost	55 per cent.

The reduction of red cells, as a rule, is not extreme, and counts between three and four millions per c.mm. are most commonly recorded. In Osler's series of cases the red cells averaged 3,425,000, with extremes of 2,187,000 and 5,200,000 per c.mm., the hæmoglobin in the same series averaged 47 per cent. with extremes of 25 per cent. and 75 per cent. Various writers have reported that they have discovered normoblasts and poikilocytes present in advanced cases; in none of my cases were these abnormal blood constituents present.

The leucocytes are also reduced—the average in Osler's cases was 3,850 per c.mm. One of my cases was remarkable for the extremely low number of leucocytes, the actual number present being 1,800 per c.mm. In some cases the leucopenia may become as pronounced as in Kala-azar, in which a count of 1,000 per c.mm. is common. Leucocytosis has been reported in very rare cases; its presence points to a faulty diagnosis, unless it occurs—

1. Owing to the onset of some intercurrent affection.
2. After a profuse hæmorrhage.

What the leucopenia is due to, we cannot definitely say. The encroachment on the lymphoid elements of the spleen by fibrous tissue, and consequent diminution of its function as a lymphoid organ, may be accountable to some extent. The more probable explanation, however, is that leucolysins are

formed in the general infective process, which takes place in this disease, and that these leucolysins dissolve and disintegrate the white cells.

There are usually other minor symptoms present, which, as a rule, are not serious. Thus, we get all the symptoms associated with anæmia—shortness of breath, tired feelings, extreme debility, irregularity or cessation of the menses in women, palpitation, and various hæmic bruits, which are sometimes well marked. There is often a sense of dragging complained of on the left side, due to the enlarged organ dragging on its pedicle and peritoneal attachments. Tenderness and perisplenitis are rare. Concomitant with this dragging sensation, vomiting and gastro-intestinal symptoms are sometimes present, as in one of my cases.

When we remember the intimate relationship existing between the spleen and the stomach, we might have expected indigestion to occur in a larger percentage of cases than it does, owing to the pressure of the enlarged organ. Constipation and loss of appetite are often present, and vomiting occurs as well. According to Banti, diarrhœa marks the transition from splenic anæmia to Banti's disease. It occurred in the later stages of my one case of Banti's disease, and the motions were loaded with the colon bacillus. Jaundice is sometimes present, and is probably always to be found in the stage with cirrhosis. It was present in my case of Banti's disease, the sclerotics showing icteric staining. Pigmentation of the skin is found in some cases; in my cases, it was only present in that just referred to. It may be diffuse or localized; it was present in my case under the eyes and breasts, and over the lower part of the abdomen. It may be caused by—

a. Irritation of the abdominal sympathetic, due to tugging and dragging of the enlarged spleen.
b. Pressure on the suprarenal capsule.
c. Internal administration of arsenic—a drug commonly used in this affection.

In advanced cases, owing to dilatation of the heart, œdema of the feet is often found.

DIAGNOSIS.

The points mentioned above make the diagnosis of this disease certain. On the other hand, several morbid conditions

present a group of symptoms closely simulating those of splenic anæmia. It has to be distinguished from the following :—

1. Tropical splenomegaly or kala-azar.
2. Myeloid leukæmia.
3. Gaucher's disease.
4. Syphilitic splenomegaly.
5. Splenomegaly associated with acholuric jaundice.
6. Thrombosis or occlusion of the splenic vein.
7. Pernicious anæmia.
8. Gastric ulcer.
9. Hæmochromatosis.

Kala-azar, a disease of the tropics, is so rarely met with in this country that it may be dismissed with a word. It resembles splenic anæmia in presence of enlarged spleen, anæmia, leucopenia and hæmorrhages, but is distinguished by the history, irregular fever, and the blood examination which reveals Leishmann and Donovan bodies.

It is of extreme importance to distinguish this disease from myeloid leukæmia, for removal of the spleen in conditions associated with leucocytosis seems to be invariably fatal (Bland-Sutton, *Address on Surgery*, Meeting of B.M.A. 1914). A blood count will readily distinguish this affection, but sometimes the characteristic blood changes are temporarily absent ("aleukæmic phase"), making it extremely difficult to distinguish the two affections. If there is any doubt, the case should be kept under observation, and numerous blood counts made until a definite diagnosis can be arrived at.

The extraordinary chronicity of Gaucher's disease together with its clinical manifestation, viz., anæmia, enlarged spleen, and leucopenia, have caused this disease to be mistaken for splenic anæmia. The distinctive features are as follows :—

1. Familial occurrence.
2. Incidence in children.
3. Characteristic yellowish pigmentation.

It is now generally held that it is a type of new growth—an endothelioma.

Syphilitic enlargement of the spleen, owing to the presence of a gumma or lardaceous disease, when accompanied by secondary anæmia renders the differential diagnosis extremely

difficult, for the symptoms closely simulate those of splenic anæmia. The diagnosis rests on—

(*a*) The history.
(*b*) Wassermann reaction.
(*c*) Antisyphilitic treatment.

The discovery in 1907 by Chaufford of the increased fragility of the red blood corpuscles in chronic splenomegalic hæmolytic jaundice has separated this affection from splenic anæmia with which it was confused in the past. It resembles splenic anæmia in the presence of enlarged spleen, and anæmia in the acquired form. It differs from it in—

(*a*) Presence of prolonged intractable jaundice ;
(*b*) Increased fragility of the red cells from some unknown cause.

Thrombosis or occlusion of the splenic vein may set up a sequence of symptoms which form an exact imitation of splenic anæmia, viz., enlarged spleen, anæmia, leucopenia, recurring gastric hæmorrhages. It is impossible, except in a case presenting a history of injury followed by the symptoms mentioned, to distinguish this condition from splenic anæmia, and post-mortem it would be impossible to determine whether the thrombosed splenic vein was the cause of the splenic enlargement and subsequent blood changes, or whether the thrombosis was caused by diseased condition of the lining membrane of the vein, set up by toxins manufactured in the infective process of splenic anæmia.

The blood picture of pernicious anæmia is distinctive, and serves to distinguish it from splenic anæmia. There is a higher colour-index, and nucleated red cells and megaloblasts are found present. This, with a much smaller spleen, as a rule, than in splenic anæmia, makes the diagnosis conclusive. In a case of exceptional splenic enlargement, the blood picture alone serves to distinguish it. Repeated vomiting of blood may suggest that the case may be one of chronic gastric ulcer—especially if the splenic enlargement is not pronounced. The presence of splenic enlargement, however, should suggest the true condition.

Hæmochromatosis presents a group of symptoms, viz., pigmentation, enlarged spleen, and enlarged liver, which show a close resemblance to splenic anæmia. It is distinguished,

however, by the fact that anæmia, if present, is usually slight, and that diabetes is a distinguishing feature in the later stages.

In the latter phases of splenic anæmia with ascites, the resemblance to cirrhosis of the liver (*a*) syphilitic, (*b*) alcoholic, is marked. This I shall refer to under Banti's disease.

TREATMENT.

No writer, so far as I know, has mentioned prophylactic measures, yet surely if this is an infective disease, as practically all writers are agreed, prophylactic measures are of extreme importance. The question whether this is a disease of the poor, as I believe, is of interest in this connection. Rolleston, who was good enough to let me have his views on this question, says, "Most of the cases I have seen have been in hospital patients, but I have seen it in the well-to-do, and considering the vast number of poor as compared with rich, I do not think that I should say that it was a disease of the poor." Osler's opinion agrees with this. He informs me that he has seen as many cases in general practice as in hospital. On the other hand, most of the recorded cases have been hospital cases. And of my three cases one was a factory worker; another a collier's wife, while the third was a general labourer. Of six deaths from Banti's disease in 1913, three occurred in institutions, and details of the other three are not given.

It would necessitate the collection of a considerable body of confirmatory statistics, before one would be justified in stating that splenic anæmia is a disease of the poor. But the facts I have mentioned certainly point in that direction, and it is what we should expect, for septic teeth and lack of proper attention to the bowels are so much more common amongst the poor and working classes than amongst the more well-to do.

The prophylactic measures then are: careful attention to the teeth so as to prevent caries, and the inculcation of the habit of daily evacuation of the bowels so as to prevent the onset of constipation with its many associated evils. We may surely hope that, in these days of preventive medicine, when the general public are being educated in the principles of hygiene, when they are being taught the elementary factors

that underlie sound health, this rare affection may become rarer still, and eventually remain a pathological curiosity of the past.

The routine treatment of a case of splenic anæmia resolves itself into four heads:—

a. Hygienic.
b. Medicinal.
c. X-ray treatment.
d. Excision of the spleen.

It is of primary importance that a person suffering from splenic anæmia should have the best hygienic treatment possible, which comprises rest, plenty of fresh air and sunshine, and good nutritious food. This often leads to considerable improvement in the general condition, and by increasing more effectively the natural resisting powers of the patient may, for a time at least, lead to a general improvement of all the symptoms. For patients with splenic discomfort, wearing a suitable belt affords considerable relief.

The drugs commonly used in this affection are those recommended in other forms of anæmia, especially iron and arsenic. Of the iron preparations, I have found the ammoniated citrate the most effective and most easily tolerated over long periods. With this I give salol internally, as an intestinal antiseptic, and a mouth wash consisting of carbolic acid and boracic acid.

Barr, writing in the *Lancet*, August 23, 1902, recommends perchloride of iron and chloride of calcium as valuable hæmatinics. As general tonics, he has found strychnine, digitalis, quinine, and caffeine useful. He recommends as well that the intestinal tract should be kept as antiseptic as possible, and to that end advocates the use of salol, benzonaphthol, and an occasional saline purge. As routine treatment, he uses a mouth wash of carbolic acid and formaldehyde. Intravenous injections of salvarsan have been tried recently, apparently with good results. A more hopeful line of treatment, perhaps, would be injections of anticolic serum.

Treatment by exposing the splenic area to X-rays is attended with diminution in the size of the enlarged spleen and improvement of the general condition. The effects of this treatment, however, seem to be temporary, so that it can

only be looked upon as palliative treatment. One of my cases (Case iii.) was subjected to this treatment, and considerable improvement followed, but as the effects were not permanent, it cannot be regarded in any respect as curative. Some writers recommend this treatment before operation, because it causes considerable diminution of the spleen, and lessens the risk of operation.

Excision of the spleen seems to be the only curative measure in this disease. It is indicated in all cases attended with profuse, recurrent, gastric hæmorrhage. Its risks are shock and fatal hæmorrhage. The steadily growing mass of statistics seem to prove conclusively that not only is the operation successful in a large percentage of cases, but that it is permanently curative. In the *Annals of Surgery*, XXIV., 1901, 19 cases of splenectomy are reported, the results of operation were as follows :—14 recoveries, 4 deaths, 1 not reported. In the *B.M.J.* 1906, p. 1273, Armstrong collected together 32 cases operated on with 22 recoveries and 9 deaths, a mortality of 31 per cent., while 1 case was unrelieved.

How removal of the spleen brings about permanent improvement in the general condition is variously explained. Those who take the spleen to be the important factor in the causation of the disease, consider the operation curative because the centre of elaboration of toxins is removed. Others point out that considerable improvement results from excision of the spleen in other conditions associated with anæmia (*e.g.*, malaria), and consider that the improvement in general condition results from the removal of a mechanically troublesome, diseased organ, as well as from the collateral circulation thereby artificially produced. The general effects of treatment, both before and subsequent to operation, must not be lost sight of—the general routine of nutritious food, tonic medication, and intestinal antiseptics must have the effect of improving the tone of the individual, increasing his resisting powers, and diminishing the probability of further intoxication from the intestinal tract.

BANTI'S DISEASE.

This disease, which was described, in 1894, by Professor Banti, of Florence, represents a terminal stage of splenic

anæmia. It presents all the clinical features of that disease, and in addition :—

1. Ascites.
2. Cirrhosis of the liver with diminution of its size.
3. Gastro-intestinal symptoms, *e.g.*, diarrhœa.
4. Muscular wasting.
5. Epistaxis and other forms of hæmorrhage.

Banti in his description of the disease describes three stages :—

(*a*) The preascitic stage, in which splenic enlargement is present, with or without anæmia.
(*b*) The transitional stage, of which the most prominent symptom, as mentioned before, is diarrhœa. Anæmia and blood changes are present, the liver shows some enlargement, and jaundice may be present.
(*c*) The ascitic stage or Banti's disease proper.

This division seems very arbitrary, and the dividing line seems too undefined, especially between stages 1 and 2, for these stages run into one another.

PATHOGENESIS.

What was said in connection with the pathogenesis of splenic anæmia holds good here. It has been thought that the cirrhosis of the liver is splenic in origin ; the sequence of events suggested is that toxins from the blood produce fibrotic changes in the spleen, which set up endophlebitis of the splenic and portal veins, leading subsequently to cirrhosis of the liver.

The similarity between the clinical manifestations of cirrhosis hepatis and Banti's disease, together with the fact that in cirrhosis enlargement of the spleen is present in 50 to 80 per cent. of cases (Klopstock), suggests that both affections have a common bacillæmic origin. The discovery by Adami of polymorphic forms of B. coli in cases of cirrhotic liver, to which I have already referred, strengthens the suspicion, and renders it probable that the colon bacillus is the causal micro-organism in both affections. The view generally held now is that poisons manufactured in the spleen are respon-

sible for the secondary changes in the liver, but the objections to this theory, already mentioned in the case of splenic anæmia, hold good here. The ascites is due to cirrhosis of the liver, and probably to some extent to peritoneal irritation in some cases.

MORBID ANATOMY.

The morbid changes present in the organs in splenic anæmia are found in Banti's disease as well, with the addition of cirrhosis (multilobular) of the liver.

CLINICAL MANIFESTATIONS.

All the clinical features of splenic anæmia are present, as well as those just mentioned.

Ascites.—If a case is tapped, this increases progressively in amount. Thus, from my patient, who was tapped eight times, 9 quarts were drawn off on the first occasion and 25 on the last. The fluid occurs in association with atrophic cirrhosis of the liver. As the fluid increases in amount, it is sometimes attended with symptoms which distress the patient —vomiting, palpitation, extreme difficulty in breathing, and the usual feeling of weight and discomfort associated with any large collection of fluid in the peritoneal cavity.

The cirrhosis of the liver is multilobular; at first, the liver is enlarged, but later it becomes shrunken and atrophic.

The gastro-intestinal symptoms largely depend on the amount of fluid; they are, vomiting, diminution or complete loss of appetite, and diarrhœa. In my patient, vomiting was marked; there was absolute loss of appetite, and diarrhœa was present.

Muscular wasting is very marked in this affection, and was presented by my patient, in whom it was particularly noticeable in the muscles of the thigh. The pectoral and scapular muscles, the deltoids, and the muscles of the arm and forearm, showed considerable wasting as well. This wasting has been attributed to vaso-motor paresis of the splanchnic area, leading to retention of blood in the portal area, with a resultant fall in general blood-pressure, and diminished supply to the rest of the body. More probably, it is due to toxins acting on the central nervous system.

Epistaxis was a marked feature with my patient and was

the only form of bleeding present. It occurred as often as three or four times a day. Various other forms of hæmorrhage have been reported, such as bleeding per rectum owing to the presence of piles, hæmaturia, and hæmatemesis.

In the closing stage, a rise of temperature is by no means uncommon. The temperature of my patient rose at the end to 103°. This was associated with profuse diarrhœa, the motions being loaded with B. coli, and difficulty in micturition—features pointing to a general invasion by the organism.

PROGNOSIS.

The prognosis is bad, a fatal result, as a rule, supervening in a few months to a year; in the case here reported, death took place in 11 months.

DIAGNOSIS.

Several affections present a group of symptoms exactly resembling Banti's disease. They are:—

1. Cirrhosis of the liver.
2. Syphilis of the liver and spleen.
3. Thrombosis of splenic and portal veins.

The similarity of cirrhosis to this affection has already been commented on, for there are presented atrophic liver, wasting, epistaxis, gastro-intestinal hæmorrhage, anæmia, and in many instances an enlarged spleen. The history of the case is the only means of distinguishing the two affections.

Syphilis of the liver and spleen presents symptoms which form an exact counterpart of Banti's disease. Diagnosis depends on

1. History.
2. Wassermann reaction.
3. Antisyphilitic treatment.

In thrombosis of the splenic and portal veins the picture is identical with that of Banti's disease, and may be impossible to distinguish from it. (*See* splenic anæmia.)

TREATMENT.

The treatment of a case of Banti's disease is the same as that of a case of splenic anæmia. Tapping has been tried without success in a number of cases. I tried it in my

patient, tapping in all eight times, but it did not check in any way the reaccumulation of fluid. This is the experience of all who have resorted to this kind of treatment (*Med. Ann.* 1904; *Lancet*, August 23, 1902) Splenectomy seems to be the only treatment which holds out any hope of a permanent cure; it is a more serious measure than in splenic anæmia, and is attended with a higher mortality (50 per cent. Banti, 56·25 per cent. Rodman and Willard (*Ann. Surg.* 1913)). Epiplopexy seems to be useful in some cases.

I append the history of my case of Banti's disease; it presented the following peculiar features:—

1. Perisplenitis.
2. Paroxysmal enlargement of the spleen during the attacks of perisplenitis.
3. Marked wasting, especially of the extremities.
4. Tenderness of the spleen on pressure.

In April, 1910, I first saw the patient (H. W.), who was an unmarried factory girl aged 19 years. She complained of severe epistaxis and general debility. On examination, I found her markedly anæmic—the splenic area showed increase of dullness on percussion, and the spleen was palpable. The lower sharp border of the liver could be felt. Over the præcordial area a functional murmur could be heard, but there was no organic murmur; there was slight ascites. She was immediately put on iron and arsenic. As she showed no signs of improvement, she was removed to the Royal Infirmary, Manchester, where the diagnosis of Banti's disease was confirmed. Here she was subjected to X-ray treatment twice weekly for about six weeks. This treatment caused considerable improvement, and she was sent home. She soon became rapidly worse—the ascites became more evident, and the spleen became progressively more enlarged, vomiting and epistaxis, too, became very distressing. About this time she began to have paroxysmal attacks of perisplenitis, attended by a peculiar feature, viz., marked increase in the enlargement of the spleen during the attack, followed by considerable diminution of its volume on subsidence of the attack; the spleen, too, was distinctly tender. Diarrhœa was a troublesome feature, and she showed considerable muscular wasting. The fluid increased so much in amount that paracentesis had to be done, and it accumulated with such rapidity that this proceeding had to be resorted to about every four weeks. Nine quarts were removed on the first occasion, 20 on the sixth, 22 on the seventh, and 25 on the eighth, which was the last occasion on which paracentesis was done. The patient died of progressive asthenia, 11 months from the date on which I first saw her. Owing to family objections, a post-mortem was not made.

TOXINS AND MASTER-TOXINS. A STUDY IN TUBERCULOSIS.

By A. WHITE ROBERTSON, L.R.C.P. & S.

THE study of tuberculosis is the study of the blood, since the study of the blood is the study of toxæmia. During the past ten years, in general and consulting practice, it has been my custom to study the blood changes in the course of disease, alike in a tropical climate and in England.

The routine for the most part has included the following estimations :—

Total red cells.—Hæmoglobin percentage. Colour index. Variations in size, contour, and behaviour of red cells. Regenerative and degenerative changes.

Total white cells. — Differential leucocyte count. Arneth's estimation of the total number of nuclei in a hundred polymorphonuclears.

At first, my study was confined to the conditions of normal blood in children and adults, in eastern and western races, and to the physiological changes associated with food, pregnancy, exercise, and altitude. The first serious researches in disease were undertaken in connection with malaria and fevers returned in error as malaria. These led to an elaborate classification of the blood-picture in the various toxin-groups encountered, so that, in course of time, a certain facility was acquired in diagnosis by simple hæmatological methods only. In this way, it became easy to separate influenza from typhoid, septic from non-septic fevers, tuberculosis from other infections, and to identify many specific fevers from one another. So long as one had to deal with one definite infection only, it was generally a simple enough matter latterly to make the diagnosis from the blood-picture.

It has been, however, primarily to my investigations in tuberculosis that I have been indebted for a wider view of

toxæmia, and from the study of plural infections generally I have recently come to advance, in a recent communication, the theory of the master-toxin.[1]

For some years now, I have used Arneth's estimation of the nuclei of the polymorph cells, not only as a valuable diagnostic aid in the recognition of tuberculosis, but as a ready and reliable means of estimating the progress, favourable or retrograde, of the patient under some one or other of the systems of treatment for tuberculous disease. In this way, I have controlled the administration of tuberculin, of I.K., of serum-therapy, and of sanatorium treatment with or without graduated exercises.

The English practitioner has not made very general use of this count, and the reasons are not, I think, very far to seek. In the first place, he has very little time for the work itself or for the tuition necessary. Then again, if this objection can be overcome, he is apt to be impatient, because it takes a considerable amount of practice before he can arrive at something approaching Arneth's figures for normal persons. Once this is achieved, he is perhaps dismayed to find a dislocation to the left, in cases in which he is practically certain that no active tubercle exists; conversely, when he is frankly suspicious from the physical signs, he gets at times a normal count. Lastly, he discovers a dislocated count in certain of the exanthemata, in influenza, and in certain other toxæmias, and is led by these to refuse to attach diagnostic value to the Arneth in tuberculosis. I would suggest to such doubters, that it is possible to explain these apparent discrepancies, and to place in a clearer light the significance of the Arneth count, if we examine the difficulties afresh in the light of a broader conception and from a new standpoint.

Let us postulate that tuberculosis is the most common bacillary infection of modern conditions of life, that but a small percentage of persons escape it wholly, and that only a comparatively small proportion of persons die from its ravages. From this it follows, that while its attack is general its power to overcome is limited. If then we can explain its method of obtaining a foothold and its subsequent dislodg-

[1] "The Master-Toxin," Address to the Hunterian Society.

ment, we shall be in better position to study those cases in which it holds its ground and ultimately overwhelms the defence.

I take the position, from the commencement of this discussion, that natural resistance to tuberculosis exists to a very high degree in mankind, and there are few diseases of bacterial origin to which he is so capable of acquiring an active immunity. Let us note first, that it is most widespread and most virulent during the working periods of life, and that it takes three or four years, as a rule, to destroy its victim, whilst many patients survive its activity for long periods of years. In addition, let us note that over 90 per cent. of post-mortems show healed lesions of undoubted tuberculous infection. Resistance in man must, therefore, be at a high level, and it must be conceded that it is only when this resistance is lowered that tuberculous manifestations appear. So long ago as 1888, in my student years, we were taught that tuberculous bone and joint affections were invariably preceded by an injury to the part affected, a blow or fall often forgotten. More recently, we can trace in our tuberculous adenoids a frequent history of throat affections; resistance locally has been in default. Of late years, I have noticed that in tubercle of the uterus and its appendages there is commonly a history of injury or displacement as an antecedent condition.

Similarly, there is, in the common experience of the profession, a very large group of infections the toxins of which have a distinctly subversive action on the production of immunity bodies. The term "sequela" is itself an admission of the potency of this, even long after the original symptom syndrome has disappeared. Otitis media, ozœna, and mastoid disease commonly follow the exanthemata on the one hand, and, on the other, measles, scarlatina, whooping-cough, pneumonia, and influenza have all figured largely in our clinical history sheets as the starting point of tuberculosis. These are master-toxins, and, so long as their degrading influence on the trophic factors in metabolism and blood activity is paramount, antibodies to all subsequent bacterial infections must be in default, and sequelæ will develop in chronicity and in defiance of local treatment, while infections, hitherto latent, tend to become

active, and new infections progress unresisted.

With these neuro-depressants are to be classed as well such others as shock, starvation, exposure, accident, operation, and pregnancy. Their influence in lowering resistance to infection is common knowledge, and their close association with tuberculosis is well recognized.

One and all, these conditions must be regarded as predisposing factors, and they all act in the same way, namely, by limiting antibody formation and so discounting resistance to bacterial invasion. Tubercle being, as I have pointed out, the most general of these assailants, is it any wonder that it commonly appears as a sequela, or that it lends its own particular factor to the blood-picture in a dislocation of the Arneth? Amongst the hundreds—nay, thousands—of blood-pictures I possess, its appearance in such conditions is always heralded by a left-handed drift in the nuclear percentages, long before there are any overt signs that the disease is active. The longer I study the Arneth picture in disease, the more I am convinced that a left-handed dislocation is direct evidence of tuberculosis active or reactivated, and that its appearance in, or subsequent to, any of the diseases I have enumerated is a sharp warning that the after-treatment of the sequela may exceed in importance the primary handling of the initial toxæmia. One should not regard any of these invasions as cured, unless the blood picture, once more restored to normal, testifies that the toxæmia is wholly gone, and that no secondary toxæmia is left to proclaim the activation of a sequela so redoubtable.

Now that treatment by specific remedies is so much the vogue, and our patients demand of practitioners a thorough familiarity with the tuberculins, with I.K., sensitized vaccines, sera, etc., it is well to consider our position with regard to tuberculosis afresh, and to ask ourselves whether the frequent disappointment and failure of all these remedies cannot be explained in terms of master-toxins—present certainly, but often, we may say generally, unsuspected. I have, of late years, devoted a great deal of time to the study of chronicity in disease, and the conclusion being forced upon me is, that in all cases of chronic disease, of bacterial origin at least, this chronicity is the index and measure of the activity of a second,

generally pre-existing, toxin, whose influence on the immunizing capacity of the blood is the cause of the failure in repair and resolution. Such toxins are to be found in syphilis, in malaria (especially of the subtertian type), and most commonly, and with even wider influence, in intestinal stasis. These three are, in my experience, the great chronic master-toxins, and no case of lasting ill-health or chronic disease can be said to have been examined carefully in which, in the evident absence of the acuter group already referred to above, search has not been made for the evidences of these in the blood.

In syphilis, we have the Wassermann reaction, and in malaria, the protozoon; but these are relatively less common factors than the toxins of intestinal stasis, and every practitioner should become familiar with the characteristic blood-picture and symptoms of this very common condition. The blood-picture is very characteristic as a rule. The red cells are normal or but slightly reduced, the hæmoglobin figure good, and the colour-index about normal. A reduction in these, especially in the two last mentioned, occurs in the later stages only, when hæmolysis is induced by the activity of streptococcal organisms. There is always leucopænia, varying from 2,500–6,000 per cubic millimetre. The lymphocytes are relatively, sometimes actually, increased, the eosinophiles persist, and the large mononuclears are almost constantly in excess. At this stage, stasis may exist with all its chronic toxæmia without constipation, though constipation is the rule.

The stool is passed daily, but it is the overplus. Should the bowel contents become liquefied by bacterial (septic-tank) action, diarrhœa or loose motions will supervene, and the blood-picture changes to one of normal or over-normal leucocyte count, with the polymorphs ranging anywhere between 70–80 per cent., or even higher. Eosinophiles are still apt to persist, and the large mononuclear excess is even more marked. These two conditions alternate, and their blood-pictures with them. If, at the same time, the Arneth index shows a normal figure—that is, 2·7 to 2·76 nuclei per neutrophile polymorph over a count of 1–200 cells—one may still exclude tuberculous activity. But the first indication of a tuberculous flare is invariably a drift to the left in the Arneth count, so that cells

with only one or two nuclei predominate, and the index per cell falls gradually as the disease progresses, till it reaches a very low figure, 2·3 to 1·8.

If secondary infections, such as pyorrhœa, antrum disease, sinusitis, neuritis, rheumatism, tuberculosis, etc., are to be handled with success, the master-toxin, and it is in practice generally intestinal stasis, must receive primary attention. Vaccine therapy (and this includes the tuberculins) owes its failures, it seems to me, to the unsuspected presence of some one of these master-toxins degrading the blood, interfering with metabolism, and subverting normal trophic regulation. Antibodies cannot be produced in adequate response, and the vaccine fails or even acts as an extra toxin. Septic and chronic inflammatory conditions persist in spite of free drainage, sinuses continue to discharge indefinitely, and invalidism and asthenia result.

In my experience of vaccine therapy, I have noted this failure to respond in many cases, until the subversive primary toxæmia was recognized and removed. I say *removed* advisedly, for I have seen coli bacilluria treated with vaccines over a period of years with only partial benefit, because the intestinal stasis, the source of the organisms, was not radically treated.

I could quote very many cases, illustrating the overwhelming influence of the master-toxin. Our common fault, as physicians, is that we do not look for these, or we are content to accept overt complications as the furthest goal of our quest. It is right, for instance, to recognize oral sepsis and pyorrhœa, or ozœna (pyorrhœa narium), as a vicious factor in the case of the tuberculous, but these in their turn are but the expressions of a greater and more general toxæmia, just as is a foul tongue in atonic dyspepsia, the common source of them all being the toxæmia of intestinal stasis. Not until this has been detected in the blood-picture, verified by X-ray examination, and radically treated by removal of the cause of the stasis itself, can we hope to restore the disorder at any given point, and bring back the condition of health to the blood—which is the life.

On a critical review of my notes of failures with tuberculins over a series of some hundreds of cases, I am very

much struck by the fact that these constantly show evidence in the blood-picture of the master-toxin, and, in cases of joint disease and empyæma with chronic sinuses, I am similarly convinced that success in treatment postulates the recognition and eradication of these first.

To return to my first contention, I believe that our present outlook on tuberculosis as a virulent primary disease is *all wrong*, and I can see no prospect of success in our national campaign against it, until the proper appreciation of the infection as a purely secondary and preventible, as well as curable, toxæmia is systematically taught. Our present anxious search for the perfect specific is, to my thinking, the merest waste of time on pithless palliatives.

The vaccines or tuberculins may have a certain value when the master-toxin is removed; but I believe, certainly in the case of tuberculosis, that recovery by natural processes may be expected after this has been effected, and I have seen this proved time and again in my own experience.

SUICIDE—FROM A GENERAL PRACTITIONER'S POINT OF VIEW.

By J. BARFIELD ADAMS, L.R.C.P., L.R.C.S.

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PROBABLY more than a third of an alienist's patients are suicidal, but being forewarned he is forearmed. With the general practitioner, it is otherwise; suicide, or an attempt at suicide, is comparatively rare in his practice, and, being unexpected, no preparations have been made to meet the emergency. Even if a suspicion of the possibility of such an act arises in the doctor's mind, he may have the greatest difficulty in inducing the friends of the patient to take the necessary precautions.

When one thinks of the distress which an accomplished act of self-destruction causes to the family of the victim, it is certainly worth while considering the subject from the point of view of the man engaged in general practice, for in many cases it is only he who has the opportunity of saving the situation. The subject is important as well, because a recognized suicidal tendency is often the principal reason, in the eyes of the public at least, for sending a patient to an asylum.

For the convenience of study, suicides might be divided into three classes: the insane, borderland cases, and the sane. But these divisions, especially the two last, shade into each other so imperceptibly, that it is often difficult to determine in which category a given case should be placed. Consequently, such a classification is only possible on paper, and would serve no practical purpose.

In dealing with this subject, one finds that patients suffering from melancholia are of the first importance. A well-marked case of this disease, complicated with delusions it may be, is easily diagnosed, and as soon as possible placed under care. But everything has a beginning, and it is a matter of common knowledge that it is in the early stages of melancholia that suicide is most likely to occur.

A possible explanation of this fact is the tendency of both mind and body to adjust themselves to circumstances even in disease. It is at the beginning that either physical or mental pain is most acute ; prolonged suffering leads to exhaustion and consequent dulling of sensibility. It must be remembered, too, that at first, and in many cases all through the course of his illness, a melancholic's reasoning powers are but little, if at all, impaired, and if one considers the horrible condition of depression and dread in which such a man exists, one is compelled to admit that, from his point of view, he acts logically in seeking the only certain means of obtaining relief from his sufferings.

Mental confusion, using the words in their ordinary sense and not as a term of classification, does not increase the tendency to suicide ; indeed, one may say that the more sane an insane man is, the more likely is he to commit self-murder.

As a matter of fact, the great majority of patients suffering from simple melancholia never attempt self-destruction ; but it is more than probable that in the minds of nearly all of them, at one time or another, the idea and even the desire to commit the fatal act is present. The notion may have been meditated upon for a long time, or it may be a sudden impulse, and there cannot be any doubt that the sight of the means of self-murder, or even the knowledge of where such may be found, is occasionally an incentive to the act. In more than one case I have felt convinced that imitation played a part in the tragedy. A patient reads the account of a suicide in a newspaper, reported, it may be, with fascinating detail, and he feels irresistibly impelled to follow where another has gone before.

With the exercise of tact and patience it is not very difficult to understand these cases, for the melancholic is generally accessible. When he is assured of your sympathy, he is not unwilling to discuss his trouble with you, though he has no hope that you will be able to help him. It is this hopelessness, by the way, which so sharply marks off the melancholic from the hypochondriacal patient. The latter has the most profound confidence in the skill of each new doctor he consults. He hails every chance word, every commonplace question as evidence of the practitioner's insight into

his obscure disease. No one more pleasantly tickles the vanity of the physician than the hypochondriacal patient in the first interview, but it must be added that no one more deeply wounds the good doctor's *amour propre* than such a man does in the later stages of their acquaintanceship.

When the melancholic has given you his confidence, it is comparatively easy to discover whether he is suffering from any delusion or from hallucinations, particularly aural ones—we all know the importance of "hearing voices"—and gradually one forms an idea of the disease, and estimates its dangers.

In these cases, as in other departments of his work, the medical practitioner has often more difficulty with the friends than with the patient. They are usually possessed with the idea that the sufferer can shake off his depression if he will, and that all he wants is rousing. So they proceed to rouse him, frequently with disastrous results.

John Bunyan, in his youth, appears to have suffered from attacks of mental depression, which possibly may at times have passed beyond the ill-defined line which separates insanity from sanity, and describes feelingly the conduct of a patient's friends under such circumstances:—"But they began to harden: they also thought to drive away his distemper by harsh and surly carriage to him; sometimes they would deride, sometimes they would chide, and sometimes they would quite neglect him."

The following case illustrates this point:—

A.B., a dressmaker, aged 30. She worked at home with her mother and sister, who were engaged in the same trade. Her father died of phthisis, and she had lost a brother and a sister from the same disease. She was dark complexioned and sallow. She looked ill, and was considerably under her weight. She slept badly, and for some months had suffered from mental depression. One morning she got up earlier than usual, went down to the back kitchen, and hung herself with the clothes line. She was, however, discovered in time and cut down.

When I asked her what reason she had for attempting to commit suicide, she told me that her mother and sister were constantly telling her that her miserable feelings were all her own fault, that she had nothing to worry about, and that she could be cheerful if she chose. At last she could bear their reproaches no longer, and, after a sleepless night, she came downstairs with the determination to end it all.

After the attempt, as frequently happens, A.B. was very much better than she had been for some time. But the improvement did not continue.

and in less than a fortnight it became necessary to remove her to an asylum. She was discharged in a few months, and remained well for two years. Then she became depressed again, and was sent a second time to an asylum, where she ultimately died of phthisis.

Incidentally, it may be noticed here that A.B.'s sister, who suffered from mitral incompetence, and who became depressed at the approach of the climateric, attempted to hang herself with a similar piece of rope in exactly the same place as her sister had done before. It is not uncommon for insane members of the same family to commit, or try to commit, suicide in the same place and by the same means as their relatives have done. These coincidences are frequently commented upon by coroners, and reported in the newspapers, as they appear to interest the public.

Usually, a melancholic's natural affections seem to be blunted. He is so absorbed in his own troubles, that he is callous to all else. He cares nothing at all about those who are nearest and dearest to him. But there are exceptions, and from a social point of view they form an exceedingly important class. In such a case, the patient's love for his wife, for his children, and for others dear to him is redoubled. The future he dreads for himself, he dreads even more for them, and the danger is that he may murder them before he destroys himself. Such a man is often most inaccessible, and his conversation and demeanour are rational to a degree.

Cases of chronic delusional insanity are by no means uncommon in general practice. The patient is often above the average in intelligence, his judgement in things unconnected with his delusion may be good, and his memory excellent. As it usually takes years for the delusion to be built up and systematized, he is frequently for a long time the last man in the world whom anyone would consider insane. But if the delusion be one of persecution, such a patient is exceedingly likely to commit suicide.

A.C., a man aged 30, who came of a highly gifted but neurotic stock, about two years ago made a determined attempt upon his life. Upon investigating the case, it became evident, both from his own admissions and from facts which had been observed by his friends and acquaintances, but not taken much notice of at the time—we were all very wise after the event—that for five years, and probably longer, he had been slowly building up a theory of persecution on a foundation of delusion. All

the time, it should be noted, he had been living his usual family life, conducting his business with success, and giving wise advice to others.

In spite of the advance of morbid anatomy and of the many accurate methods of diagnosis, which the modern alienist employs, the general practitioner has still to rely almost entirely on mental symptoms in dealing with the cases of insanity which occur in his practice. At this point, I may perhaps be permitted to observe that dread (including under this term both apprehension and anxiety, though not giving to the latter word all the extension with which it is used by some French writers on psychiatry), in the sphere of the emotions, as among the melancholics, and ideas of persecution in that of the intellect, as among the paranoiacs, appear to be the principal indications of a tendency to suicide.

It will often be found that in the earlier stages of his disease, a patient suffering from chronic delusional insanity is very inaccessible. He may be naturally a proud and reserved man, and when first the idea that he is shunned or despised by his fellows creeps into his mind, his pride is hurt, but he would not for the world reveal his injured feelings to another. Later on, however, when he has begun to theorize, to fit explanations to everything he thinks he sees or hears, and especially if his delusion has become tinged with ideas of personal importance, he may be ready to discuss his trouble with anyone in whom he has confidence, or who he thinks can protect him, or help him to avenge himself upon his imaginary persecutors. He may, of course, proclaim his wrongs from the housetop, claim the protection of the police, or take legal action in self-defence. But I am speaking of the less obvious cases, for it is especially in these that the general practitioner, by early recognition of the condition, may save the man from suicide.

At whatever stage of his disease one can get such a patient to discuss his delusion, one is struck with the fact that however great his trouble may be, and however completely it occupies his thoughts, he is never so profoundly depressed as a melancholic. The latter has given up hope; the former will make a fight for it, and he is often as ready to kill those, whom he believes to be his persecutors, as

he is to take his own life. Consequently, the man who suffers from chronic delusional insanity is always a potential social danger.

Among the epileptics, who are met with in general practice, there are two classes of patients which are especially prone to develop a suicidal tendency. A typical representative of the first class is a man on whose mind the fact that he is an epileptic, and that, consequently, he is prevented from taking his proper position in the world, has begun to weigh heavily. The intelligence of such a man is frequently above the average, and possibly the acuteness of his reasoning powers, which distinguishes him from his fellow sufferers, may increase the danger of his taking his own life.

In the second class are those patients in whom the long sleep, which so frequently follows the fit, is replaced by a condition of more or less mental depression. In two cases, which I have recently had the opportunity of observing, the post-epileptic state was not marked by any mental confusion, but approximated very closely to simple melancholia. It was difficult to get either of the patients to discuss their feelings, but, as far as one could make out, both suffered from profound dread of another fit, and one of them certainly felt keenly the effect of his disease on his social position. This would connect his case with the class of epileptics mentioned above.

It is unnecessary to dwell upon the possibility of suicide in cases of puerperal insanity. Before the mental symptoms have become serious, the patient is usually under the observation of a doctor or a skilled nurse.

The danger of attempts at self-destruction occurring during the delirium of acute diseases, is one which cannot be overlooked. The following cases will illustrate this point :—

A.D., male, aged 45, was suffering from acute rheumatism with hyperpyrexia. There was the history of two previous attacks of the disease, one having occurred in childhood. He had an old mitral pre-systolic. He was delirious, but the condition of his joints appeared to render him helpless. However, in the temporary absence of the nurse, he managed to crawl to the bedroom window, throw himself out, and kill himself.

A.E., male, aged 38, suffering from erysipelas. Delirium continued for some days. Made two attempts at suicide. The first attempt was nearly successful, for the patient succeeded in overpowering the nurse, but fortunately help arrived in time. The second attempt, being expected

was more easily dealt with.

In the case of this man, the dream-like nature of the delirium was very evident. In his attempts at suicide, he seemed to take hardly any notice of obstacles animate or inanimate, his whole attention being fixed upon the means of self-destruction. The mental condition reminded one of that which is observed in delirium tremens. The concentration of the patient's mind on the one idea and his blindness to his surroundings were in marked contrast to the intelligent way, in which some melancholics set about taking their own lives.

Alcoholics bulk largely among the clientèle of the general practitioner. Without midwifery and the results of drink, some of us would have very little to do. It is universally recognized that, next to heredity, alcohol is the commonest cause of insanity, and it follows that it is a common cause of suicide.

The two conditions of alcoholism, met with in general practice, in which suicide is most likely to occur, are delirium tremens and dipsomania. In the first, experience has taught one to be more suspicious of the patient who suffers from aural hallucinations, than of the one in whose case they are purely visual or visual mixed with tactual. That is to say, that a patient suffering from delirium tremens may see the most frightful objects, may see all manner of creeping things, may even feel them crawling over him, and yet be less of a danger to himself than one who is comparatively quiet and "hears voices."

The same observation applies to cases of dipsomania, during the stage corresponding to delirium tremens. But in this disease there are other dangers. In several patients, I have noticed a strong tendency to suicide during the period immediately preceding the outbreak of drinking. A dipsomaniac is often a conscientious man, and fights manfully against the impulse to drink when he feels it creeping over him. He is fully aware that the disease, from which he suffers, jeopardizes his social prospects and the happiness and, it may be, the future of those dependent upon him. His condition is truly pitiable, and I fear that we do not always give him credit for the efforts he makes to conquer, before he finally yields to the

craving. It is in this stage that there is a danger, and a very great danger, of suicide; it is then that help is most needed. Yet how are we to give it?

From the point of view of the subject of suicide, the various obsessions and phobias, which we meet with among our patients, are of importance according to the amount of mental depression and anxiety they are capable of causing. There is one of them, however, which stands out in high relief, and that is the fear of the results of syphilis. The dread that a man, who has suffered from this disease, has of communicating it to his wife or children is, perhaps, one of the most horrible that can take possession of the human mind. I have seen three such cases recently, and they have impressed me with the fact that no patient is so likely to commit self-murder as a syphilophobic.

The conditions, which I have briefly touched upon above, may all be said to occur among the insane, or in patients who may be grouped under the head of borderland cases. May I be permitted to add a few words on the subject of suicide among the sane?

Does it ever occur?

In "Le Détour," one of Bernstein's earlier plays, a healthy young woman, who for months has suffered acute mental anguish, and whose future appears to be as black as it is possible to imagine, says:—"Certainement, à ma place, une imbécile se tuerait." That, I believe, is the view of the idea of self-destruction, which every normal man or woman would take even in the worst circumstances. Self-murder is opposed to one of the strongest of animal instincts. If it were possible to examine carefully the mental condition of all suicides before the fatal act was committed, one would probably be compelled to endorse the commonplace verdict of the coroner's jury—"temporary insanity"—in the vast majority of cases.

Still, I suppose, there are few of us who have not known one man, at least, who of his own free will and in full possession of all his faculties has stepped through the door, which Epictetus told his disciples was always open; though, indeed, the Stoic bade his hearers hesitate, and not depart without a cause.

For these unfortunates we can do nothing. But there is a

class of men, who are tempted to destroy themselves, and who sometimes carry the impulse into execution, that we can help. In these cases the trouble is as much, if not more, physical as mental.

We are taught to look with caution upon overwork as a cause of insanity, and no doubt such teaching is wise. But I think every general practitioner will admit that overwork with its consequent fatigue, insomnia, loss of appetite, and above all when it is complicated with anxiety, may even in the healthy lead to a mental breakdown, which, unless treated, has often the most disastrous results. In the professional and commercial classes, it is not uncommon to meet with those who wilfully overwork themselves. They take little or no recreation, neglect their regular meals, and encroach largely upon the necessary hours of sleep. Indeed, such a man often boasts of his power of doing with less sleep than his fellows, being ignorant that the mere fact, that his nervous system does not register fatigue in a normal way, is evidence that there is something wrong in his make up. Under the strain of some extraordinary anxiety, or when his exhausted brain loses all just sense of proportion and he makes mountains out of mole-hills, is it a wonder that such an individual breaks down?

We all know the popular remedies for such a condition—drugs, generally in the tabloid form, to woo back offended sleep, alcohol to whip up the jaded neurons, and, if all else fails, travelling is suggested, one form of fatigue being substituted for another.

A little later, and the world is astonished at hearing that the sane business or professional man has taken his own life. Ever ready to find a cause for every event, the world whispers something about financial embarrassments, a double life, etc. But the man's affairs are found to be in perfect order, and his family life has been as happy and honourable as possible.

I venture to think that a medical man could have saved such a case, if only the patient would have followed his advice.

Practical Notes.

SOLUTION FOR RECTAL AND INTRAVENOUS INJECTION.

Schiassi points out that the use of the ordinary normal saline solution for rectal or intravenous injections occasions loss in the calcium and potassium contents of the tissues, especially in the nerve tissues. A reduction of 50 per cent. in the case of calcium has been recorded, and the loss of this tonic element has brought about a very depressant effect. He has made a series of clinical observations, and has found that by reducing the amount of sodium chloride, and adding calcium and potassium, a tonic effect is obtained and the coagulability of the blood is increased. To counteract the acidosis frequently produced by surgical operations, he adds sodium bicarbonate, and glucose is included as well, on account of its diuretic effect and general tonic action, particularly on the heart.

For intravenous injection, he uses :—

Sodium choloride (pure) - - -	6·50 g. (gr. c.)
Potassium chloride - - -	0·30 ,, (gr. v.)
Calcium chloride (fused) - -	1·00 ,, (gr. xv.)
Sodium bicarbonate - - -	0·50 ,, (gr. vii.ss.)
Glucose - - - - -	1·50 ,, (gr. xxiv.)
Distilled water - - -	1000·00 (℥ xxxv.)

For rectal injection, he increases the amount of glucose to 50 g. (℥ iiiss.) and adds 15 g. (℥j.) of pure ethyl alcohol. He considers that rectal injection is preferable, because the substances absorbed are carried by the portal system to the liver, and are there properly transformed for use. The alcohol promotes the flow of the fluid through the mucous membrane of the gut, and increases its powers of diffusing.—(*La Semaine médicale.*)

TREATMENT OF GANGLION BY INJECTION OF TINCTURE OF IODINE.

This method was introduced by Duplay many years ago, and is usually referred to in the text-books as of historical interest only. Robineau, in 1929, recognized its merits, to which again Pakowski draws attention after having used it in many cases with complete satisfaction to his patients and himself.

An hypodermic syringe with a short needle is required. The back of the wrist is painted with tincture of iodine. The palm is placed flat upon the table. If the ganglion is not very prominent, it may be made more so by resting the forearm only on the table, and allowing the hand to hang over the edge. The cyst is then immobilized between two fingers of the left hand, whilst the needle is thrust into it by the right. There is very seldom any fluid issuing from the cyst. Two or three drops of tincture of iodine are then injected into the cyst, and the needle withdrawn. If, as occasionally happens, a few drops of cystic jelly exude, stained with the

iodine, Pakowski advises the injection of a few more drops into the cyst Light compression by a dressing, kept in place by a few turns of bandage, is applied, but it must not interfere in the least with the movements of the hand or the fingers. It is left in place for three or four days, when, as a rule, the cyst will be found to be very much smaller or to have disappeared entirely. A second injection is needed in some cases, and neither Robineau nor Pakowski has ever seen a ganglion resist three injections. The only painful part of the proceeding is the prick of the needle; for a few hours after the injection, there is a feeling of heat and fullness in the hand.—(*Journ. des Practiciens*, 20 June 1914.)

FOR IMPETIGO.

Gougerot points out that the small, round, scaly areas on children's faces (dry impetigo, pityriasis faciei) are due to streptococcal infection and are not a form of eczema. The fact is established by Sabouraud's researches. At first, the face should be washed with boiled water, containing either borax or bicarbonate of soda. The soap then used for washing should contain borax and coal tar, and afterwards some cold cream or glycerine of starch should be applied.

If this is not successful the following solution should be applied on swabs of absorbent wool:

℞ Acidi Salicylici - - - - - gr. xv.
Spiritus Rectificati - - - - - ʒiiss.
Aquæ sterillizatæ - - - - - ʒiij.
Misce. Fiat lotio.

The following ointment should then be applied:—

℞ Hydrargyri Subchloridi,
Acidi Tannici - - - - ana gr. v.
Paraffini Mollis - - - - - ʒj.
Misce. Fiat unguentum.

The amount of soft paraffin may be reduced to obtain a more active ointment.

In obstinate cases, ointments containing sulphur, coal-tar, or cade oil are required. The following is useful in seborrhœic eczema as well:

℞ Hydrargyri Oxidi Flavi - - - - - gr. xv.
Picis liquidæ - - - - - ʒiss.
Paraffini mollis - - - - - ʒivss.
Misce. Fiat unguentum.

—(*Le Progrès medical.*)

Reviews of Books

Elements of Surgical Diagnosis. By Sir Alfred Pearce Gould, K.C.V.O., M.S., F.R.C.S., Surgeon to the Middlesex Hospital, assisted by Eric Pearce Gould, M.A., M.Ch. Oxon., F.R.C.S. 4th Edition. Pp. 723 with 10 Radiographic Plates and 14 Figures. London: Cassell and Co., Ltd. 10s. 6d. net.

Eleven years have passed since the last edition of this work was issued, and much modification has been required, due to the advances of surgery in the interval. The same general features persist in the book, viz., the diagnosis of injuries and diseases are kept separate, and the main descriptive parts are regional rather than general. It is needless to say that the present issue maintains the high position of this work and it will be of the greatest value to students and practitioners alike. The introduction of a few illustrations, and of an admirable series of radiographic plates will also enhance its worth. Amongst the latter there are some excellent radiographs of bismuth meals, and a few illustrations of pyelograms, which abundantly testify to the value of pyelography.

A detailed review of a work such as this, which has a well established reputation, is unnecessary. We would, however, especially note the excellence of the section devoted to abdominal lesions, which has been improved by the addition of short chapters on the diagnosis of the more important sequelæ of abdominal operations, and another on the diagnosis of some causes of chronic indigestion. The latter, we are sure, will prove to be one of the most useful addenda in the work.

Rose and Carless's Manual of Surgery for Students and Practitioners. Ninth edition. Revised by Albert Carless, M.B., M.S., F.R.C.S. Pp. XII + 1408. London: Baillière, Tindall and Cox. 21s. net.

We find it a matter of some difficulty to review such an old friend. Since the first edition published in 1898, there have been no less than eight English editions, four of them reprinted; four American editions, three of them reprinted; one edition each in Hungarian, Chinese and Arabic.

What "Rose and Carless" was to most of us as students, "Rose and Carless" is to the student of to-day, the invaluable rock on which to build the full knowledge of surgery. The edition before us is no bigger than the one we read as students, yet it contains everything the student of to-day requires, and almost all the practitioner of to-day will find of use. There is no padding anywhere; the story is simply and clearly set down, and the illustrations, many of them beautifully coloured, are very numerous and of the greatest utility. The new chapters on modern methods of treatment by heat, light, electricity, and radium, is a most useful adjunct to the book, and brings it fully up to date.

We would (1) criticize the offhand treatment given to Crile's Anoci-association, which teaches a the very least the most important and

necessary fact, that because a patient is under chloroform or ether it does not mean that he cannot "feel," and thereby indicates that an important and vital factor to be borne in mind, by an abdominal operator especially, is gentleness in handling tissues; (2) complain, on behalf of practitioners, of the very terse description given to what the book calls "Appendicular Gastralgia." There can be no doubt the condition is exceedingly common, and is becoming rapidly recognized. The statement that "the condition of the appendix probably causes intestinal stasis, and this in turn sets up a toxæmia which reacts on the gastric mucous membrane" is surely very far from being proved.

We may say most cordially that there is no text-book of surgery in this or any other country so adequate and yet so convenient for the student of surgery.

The printing, the production of the illustrations, and the binding reflect the greatest credit on the publishers.

We may add with interest that this is the only book we are taking with us to the "front."

Eye, Nose, Throat and Ear. A Manual for Students and Practitioners. By James Forrest, M.B., Ch.B. Pp. 403. London: Henry Kimpton. 10s. 6d. net.

The author, in a preface in which the first and third personal pronouns are curiously mixed, has compiled a concise work in which unessential theoretical considerations have largely been dispensed with. Much space, however, has relatively been allotted to errors of refraction and their associated conditions, the author maintaining that every practitioner should be a competent refractionist. The portion relating to diseases of the throat, nose, and ear, is adequate, although greatly condensed, but this is, in some measure, corrected by numerous illustrations, some of which are in colour. The work will probably find a place as a short and concise handbook for the general practitioner and the student. More than half the pages are devoted to the eye and its diseases, and the descriptions and directions are sufficiently clear for the average reader, but it is in no sense a work that can be ranked as a text-book.

Text-book of Local Anæsthesia. By Prof. Dr. Georg Hirschel, Heidelberg: translated by Ronald E. S. Krohn, M.D. Pp. 181. London: John Bale, Sons, and Danielsson. 8s. 6d. net.

It is extremely doubtful whether the methods, described in this work, will ever replace general anæsthesia in this country to the extent they are now doing in Germany. In skilled hands, general anæsthetics administered by modern methods are applicable in the large majority of cases, more conveniently and probably quite as safely as some of the "looping the loop" methods herein described. Nevertheless, a text-book covering the whole field of infiltration and conduction anæsthesia, with references to the literature of the subject, may serve a useful purpose.

The present volume, it must be confessed, is a little disappointing. It certainly covers the whole ground; the arrangement and index are both good; it is profusely and beautifully illustrated (over 100 plates); in spite of all this, there is a lack of clearness in the description of some of the methods, which is irritating. The modern anatomical terminology, adopted

by the author, is for the most part cumbersome, and has an unfamiliar ring to English ears. Two sentences may be given as typical of many throughout the book; on page 43 (d.) "The needle viewed from the front, should point exactly to the pupil of the eye of the same side, viewed from the side to the articular tubercle of the malar"; and on page 94: "Four points of puncture are indicated in the centre of the inter-costal spaces next to the rib that is to be operated upon." On page 39 "paresis" should surely be "paræsthesia", "shall" frequently appears for "will." On page 126, the doses given by Schlimpert are mentioned in figures only, the reader being left to guess what measure or weight is intended. On page 144, the following sentence occurs: "The space between the two Esmarcks should not be less than 25 cm. (one to three handsbreadths)"—the hand of the German surgeon should inspire awe!

Everywhere, the author decries general anæsthesia, and belauds the local methods. He appears to have no knowledge of the ease and safety with which big operations on the jaw and tongue can be done, under a general anæsthetic properly administered; on the other hand, he is entirely blind to the risks involved in many of the procedures he so lightly advocates.

The Practice of Surgery. By Russell Howard, M.S., F.R.C.S. Pp. 1,228. London: Edward Arnold. 21s. net.

In the preface to this new work on surgery, the author says: "This text-book on surgery has been written at the request of many past and present students of the London Hospital, and it embodies as far as is possible in a text-book the Surgical teaching received by the writer at that medical school. The main objects of the book are to give the student an introduction to surgery, and to prepare him for the final examinations in that part of the medical curriculum; but, as special emphasis has been laid on diagnosis and treatment, it is hoped that it will prove useful to him in his career after leaving hospital work."

We would suggest that the book will become popular rather in the local than the general sense. It is lacking in two great essentials for its establishment as a student's text-book:—(1) The material, though well written, is overcrowded: and (2) the illustrations are not always good. It is somewhat of a shock to find a modern author advocating the use of marine sponges, though otherwise the description of surgical cleanliness is excellent. Whilst very properly recommending removal of the appendix in most cases, when gastro-enterostomy is performed for ulcer in the duodenum or the pyloric end of the stomach, the author is surely in error advocating the middle line incision. It is certainly better, both with a view of treating the pylorus by infolding and closure, and with a view of removal of the appendix, to make the incision to the right of the middle line. In view of the greater importance of duodenal ulcer, we would criticize the prominence given in every way to gastric ulcer. That portion of the book devoted to orthopædics and to bone surgery is most excellent, and the classification of tumours on page 214 is very good indeed.

Illustrations 13-14 and 139 are indistinct, No. 30 represents nothing which could give a student any idea of an anthrax pustule. Nos. 440 and 443 cannot surely represent typical instances of "carcinoma of the tongue," and "chronic enlargement of the tonsils," respectively.

Preparations, Inventions, etc.

PONOS BISCUITS AND PONOS FINGERS.

(London: Messrs. Callard and Company, 74, Regent Street, W.)

These preparations will be found to be, what is, or used to be, very unusual in diabetic foods, extremely palatable for use with butter, cheese, and so forth. As will be seen from the following statements, one of which is printed on each box, they contain a definite but small proportion of carbohydrates:

Ponos Biscuits.		*Ponos Fingers.*	
Proteids	64·55	Proteids	66·20
Carbohydrates	2·05	Carbohydrates	1·60
Moisture	4·05	Moisture	3·50
Fat	23·25	Fat	21·00
Mineral Matter	6·10	Mineral Matter	7·70
	100·00		100·00

The necessity for carbohydrates in the food of diabetics is now recognized in treatment, if the patient is to be kept alive. Once the amount of carbohydrate tolerance for each patient has been determined, the quantity to be allowed can then be prescribed definitely, and it is a very great help to know the exact proportion present in the foods given. Messrs. Callard's preparations have always been thoroughly dependable in this respect, and our independent analyses have shown that the food's contain actually what is claimed and stated. Too many so-called "diabetic" foods or "gluten" preparations contain large amounts of carbohydrate, and are a hindrance, if not a danger, in the treatment of diabetes.

We heartily recommend these new preparations of Messrs. Callard.

ORGANOTHERAPY PRODUCTS.

(London: The British Organotherapy Co., Ltd., Carlton House, Lower Regent Street, S.W.)

A new brochure has just been issued by the Company which contains a concise summary of the latest information regarding the effects of these modern productions, as well as lists of the conditions in which it has been shown that they can be used with advantage. The list of authorities consulted for information is long, and includes every name that has been associated with this new development in treatment. A copy of the brochure will be sent, on application, to any medical man mentioning THE PRACTITIONER.

MERSALV.

(London: Messrs. M. Bresillon & Co., Gamage Buildings, E.C.)

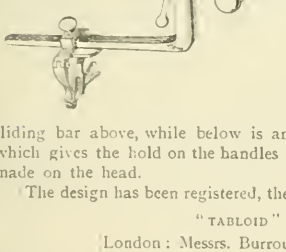
This preparation contains 10 per cent. of metallic mercury, in the most minutely divided condition possible to obtain. It has a white creamy consistence and appearance, and has a pleasant camphoraceous smell. As it

contains no organic fats or oils, it is very cleanly for use, and so is possessed of a very great and definite advantage for the inunction method of treatment. This has long been known and recognized to be by far the most effective and effectual method of treatment by mercury, but it has always been most objectionable in use, being dirty, greasy, and prone to cause irritation. Clinical experience with mersalv has proved that its use is quite free from objection, and that the mercury is entirely absorbed by the tissues, with the result that the patient is brought more quickly under its influence. About one drachm is used for inunction, and this amount has practically disappeared, leaving the skin dry, after a few minutes' light rubbing in. The combined treatment of syphilis by salvarsan and mercury now holds the field, and this preparation offers an eminently satisfactory method for carrying out the mercurial part of the treatment. Mersalv is supplied in pots containing sufficient for 15 and 30 days' treatment.

ADAPTABLE AXIS TRACTOR.

(Birmingham: Messrs. Salt and Son.)

Dr. Cuming has designed an ingenious, adaptable axis tractor, which can be fitted to any ordinary pair of forceps. It is on the principle of Neville's axis-traction, but possesses an indicating needle to show the direction of traction, and a sliding bar to allow the direction of traction to be altered.



The advantages claimed are: that it is not complicated and there are not many parts to get lost or damaged; it takes up very little room in the bag; and it is easy of application.

The traction handle is fitted with a swivel, allowing the head to make its own rotation. The instrument is fixed to the handles of the forceps by means of a screw on a sliding bar above, while below is an adjustable grip fixing with a screw which gives the hold on the handles and regulates the amount of pressure made on the head.

(The design has been registered, the registered number being 645,369.)

"TABLOID" HEXAMINE.

(London: Messrs. Burroughs Wellcome & Co.)

In the new edition of the British Pharmacopœia, this name has been assigned to Hexamethylenetetramine, the drug being added to the official list. This powerful urinary antiseptic, diuretic, and uric acid solvent is now being manufactured at the Wellcome Chemical Works in England, and is issued in "tabloid" form in 3-grain and 5-grain sizes. The product conforms in all respects with the tests and character of the P.B. 1914. The "tabloids" are put up in bottles of 25 and 100.

"ECONOMIC" ANTISEPTIC WATERPROOF.

(London: Messrs. James Spicer and Sons, Limited, 50, Upper Thames Street, E.C.)

This material has been prepared specially to meet the demand for an

economical and thoroughly antiseptic waterproof sheeting to take the place of oiled silk and macintosh sheets. We find this paper like material answers the purpose admirably. It has the appearance and light weight of paper, but it is surprisingly strong, resisting attempts of considerable force to tear it, when these are made steadily and not with a sudden jerk. It has a perfectly smooth surface, which does not roughen in the least when rubbed well after being thoroughly soaked in water. It is extremely pliable, becoming more so when well wetted in water, and it does not crinkle. It is quite waterproof. The material, therefore, is thoroughly well adapted for use for all purposes in which oiled silk, gutta percha tissue, macintosh sheeting, jaconet, and the like, are usually employed. It can be obtained in rolls, 250 yards in length, and 35 in. or 70 in. in width, at a price (3½d. a yard) considerably lower than that of the materials usually employed.

"MELARTO" CIGARS.

(London: Messrs. Melbourne Hart & Co., 19, Basinghall Street, E.C.)

These cigars are, we understand, a new brand, manufactured in England, and consist of a combination of Havana and other tobaccos, carefully selected and blended. It is claimed that, from the method of manufacture and the character of the leaf employed, the cigars contain a minimum of nicotine, and accordingly are suitable for cardiac patients who would otherwise be "warned off" smoking altogether.

On trial, we find the "Melarto" Cigars to be well made, of delicate flavour and pleasing aroma. They smoke easily and evenly, and create a white firm ash. Altogether, whilst suitable for the ordinary individual, the "Melarto" might be allowed to selected "heart" patients. The prices are much below those for the usual Havana Cigars.

POSOLOGICAL TABLES OF THE BRITISH PHARMACOPŒIA, 1914.

(Manchester: Messrs. Jewsbury and Brown, Ardwick Green.)

These tables give the comparative doses and strengths of the various official preparations in the Pharmacopœias of 1898 and 1914. The doses of the 1914 issue are given in metric and Imperial measures. The booklet is in very handy form, and the type is clear and plain. No information on the point is given, but we imagine that a copy will be sent to practitioners on application.

THE PRACTITIONER.

APRIL, 1915.

TESTICULAR TUBERCULOSIS.

By JOHN STEPHEN McARDLE, M.Ch., R.U.I., F.R.C.S.I., etc.

Professor of Surgery, University College, Dublin; Surgeon and Lecturer on Surgery, St. Vincent's Hospital; Consulting Surgeon, Temple Street Hospital and National Maternity Hospital, Dublin, etc.

[With Plates XXXIX.-XL.]

Before I discuss the life history of testicular tuberculosis, I wish to remind the reader that the sexual function of the testis is not the only one to be considered. The external secretion of that gland is not the only one which renders the gland of importance to the well-being of the subject, for while in the lower animals, such as horses, emasculation has few, if any, ill effects, in man it produces a profound mental impression, at times of an alarming nature. Mental weakness, and even mania, have followed in the track of castration carried out for the relief of prostatic trouble and for bilateral affections of the testicle. Interference with the external secretion of the testicle (semen) can hardly be the cause of the changes that have been noted after castration, and we are driven to the belief that an internal secretion is manufactured in the cells of the testicle, and carried to the brain and other body tissues through the medium of the blood.

This thought has much influence on the modern treatment of diseases of the testicle, as will be seen in the course of this paper. There are many aspects of the subject of tuberculosis of the testicle demanding and well deserving deep study. There is the question of direct transmission to the mother; there is the further thought, will dissemination through her blood lead to an hereditary taint in the progeny?

For the present, we may forego a discussion of these subjects, while the surgical aspects of the matter in hand are being

dealt with.

The affections, which most simulate tuberculosis of the testicle, are syphilis of that organ and gonorrhœal epididymitis.

The differential diagnosis is rarely difficult, for in tubercle the epididymis is the primary centre; in syphilis, the testicle proper is the point of deposition of the infective material.

In tubercle, the testicular substance is usually encroached upon only by pressure, as depicted in Fig. 1, which shows a late stage of tuberculosis of the epididymis, the testis proper being protected from invasion by the dense fibroid tissues of the rete, but compressed to a third of its natural size by the enveloping mass of tubercle, which is breaking down with abscess formation at its centre. A small hydrocele is associated with the globus major. In syphilis, the testicular substance is destroyed early and by direct infiltration, as shown in Fig. 2, an instance of syphilitic sarcocele.

Early diagnosis is essential to surgical success. The treatment of tuberculosis of the testicle has so changed in recent times that any delay in diagnosis is quite unpardonable. Some time ago treatment was palliative, now operation is at once carried out according to the conditions found, as follows:—

(1) If the tuberculous matter is confined to the globus major or minor, removal of the nodule suffices, and the resulting cavity should be obliterated by sutures of the finest catgut, the buried visceral layer of the tunica vaginalis being closed over the globus by the same material.

This operation should be carried out by cutting through the parietal tunica vaginalis, thereby reaching the site of trouble by a bloodless as well as a safe route.

(2) *Epididymectomy.*—When the entire epididymis is engaged, it should be entirely removed, taking care not to injure the blood supply to the testis, at its upper and inner side close to the globus major. The vas should be cut above the level of the testis, and if sound implanted by catgut suture into the testicular substance. The wound left by the removal of the epididymis should then be closed by suture of the tunica albuginea over the rete testis.

(3) *Castration.*—Should the tuberculous invasion extend through the fibro-vascular rete testis into the testicle proper, there is only one procedure justifiable, and that is removal

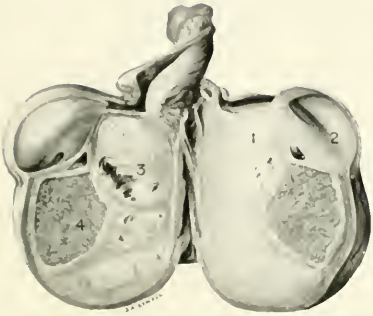


FIG. 1.—1. *Primary nodule.* 2. *Hydrocele of tunica albuginea.* 3. *Breaking down into abscess.* 4. *Compressed testicle.*

FIG. 2.—*This specimen shows the entire organ destroyed by gummatous deposit. There was a virginal hydrocele present in this case.*

Fig. 3.—1. *Primary nodule.* 2. *Miliary tubercles in body of testes.* 3. *Atrophied globus minor.* 4. *Cyst in rete testis.*

Fig. 4.—*In this case a vaginal hydrocele has* [illegible] *the deposit of tubercle in the globus minor. The combined influence of these troubles has caused an atrophy of the testis.*

of the entire organ and as much of the vas deferens as possible. All infected scrotal tissue should be removed; and into the cavity thus formed a mass of paraffin, the shape and size of a normal testicle, should be imbedded and held in position by a purse-string catgut suture. The higher up this mass is fixed the better, for there is a tendency for it to drop deep into the scrotal tissues as time goes on.

Fig. 3 represents a case in which only the last procedure could prove of any service. It will be seen in this specimen that, while the primary nodule is confined to the globus major, the body of the organ shows miliary tubercles destroying the secreting substance; at the same time, the globus minor is atrophied, and there is a small cyst of the epididymis. This condition is not usual in adults, unless associated with peritoneal tuberculosis; indeed, early miliary tuberculosis of the secreting portion of the testicle indicates systemic tuberculosis.

In the treatment of these cases the question often arises: "What should we do with the seminal vesicle, when there is thickening of that part, and the urine is cloudy with mucus and sometimes blood?" The answer is, that in nine cases out of ten one or other of the operations above-mentioned will relieve all vesical symptoms.

There can be little doubt that tuberculosis of the testis may have its origin (*a*) from the primary lesion of the bladder or prostate extending along the vas, (*b*) from the lymphatic area, or (*c*) direct from the blood stream.

As regards the first method of invasion, it must be rare, for very few cases show signs of bladder trouble, until the testicular disease is far advanced, and when the local lesion is dealt with the vesical symptoms usually subside. This could not be so, if the primary lesion happened to be a bladder tuberculosis, for this disorder is very intractable.

That the infection is conveyed by the lymph channels is hardly likely, for the flow of lymph is in a direction away from the seat of disease. These lymph vessels may, and no doubt do, convey bacilli from the disease-centre in the testicle to the retro-peritoneal glands up to the level of the renal veins, where often large nodules are found; but, in the other direction, such extension must be extremely rare, so that we

are driven to the conclusion that by far the most frequent mode of invasion is through the blood stream, as in the case of tuberculous osteomyelitis.

The terminal arteries in the epididymis are so fine that, given a local condition favourable to the growth of tubercle, such as follows slight injury, subsiding gonorrheal infection, or lowered vitality after fevers, it is easy to understand the frequent occurrence of nodules in that structure.

In children, it is usual to find the testis proper engaged, the disease runs a rapid course, the caseous deposits breaking down and bursting through the skin leaving discharging sinuses. Hernia testis often occurs, some of the parenchyma with the tuberculous granulation tissue protruding through the tunica albuginea and eroded skin. There should be no enucleation of the testicle in children.—1st. Because in the event of the trouble destroying the second testicle the development, physical and mental, of the child would be seriously interfered with; 2nd. In children many cases of this affection are secondary to pulmonary or spinal tuberculosis; 3rd. Many cases of spontaneous cure have been recorded after simple curretting away of the caseous centres the patients ultimately becoming quite robust.

I am disposed to agree with the following propositions of Jacobson and Rowlands:—

(1) When erosion fails in lesions still limited to the epididymis. If one or more discharging fistulæ still persist here, especially if the patient is not in a position to avail himself of a repetition of erosion and delay, castration should be performed, slight as the mischief appears to be, especially if they affect the patient's health or interfere with the outdoor exercise so necessary in these cases. It is only too probable that minute deposits are already making their way into the testicle itself by spreading along the rete, a condition impossible to recognize by external manipulation.

(2) When after erosion any fistula has healed, but careful watching of the patient, always to be insisted on, detects the existence of, it may be, slight but persistent swelling in the scrotum, with night sweats and loss of flesh. These may point to mischief in the remains of the sexual gland, and not necessarily to disease in the prostate, etc., or in the

lungs.

(3) When the body of the testicle is involved. When this remains enlarged, and liable to attacks of inflammation, castration should be performed.

(4) When the testicle remains atrophied and riddled with fistulæ, one or more of which persists in discharging, removal of a useless and dangerous organ should be practised.

(5) When a hydrocele is present, especially if purulent. When both testes are involved, it is rarely justifiable to remove the two. In young subjects, the worse may be removed, and the diseased epididymis and vas deferens may be excised on the less affected side, the testicle being saved for its internal secretion.

The palliative treatment by injection of iodoform glycerine emulsion, first recommended by Senn, has often proved of great service, and so has the parenchymatous injection of 10 per cent. zinc chloride solution, advocated by Lanalongue.

Tamponing with iodoform gauze, after scraping and brushing the scrotum with 2 per cent. alcoholic solution of iodine, is sometimes successful.

It is necessary in all these cases to secure an outdoor life, with good hygienic surroundings and proper food.

The best drugs to aid us in the drying up of discharges are lactate of calcium internally, and locally a solution of acetate of aluminium (30 grs.—℥j.).

Occasionally, tubercle in the epididymis is associated with a vaginal hydrocele, as shown in Fig. 4 (Plate XL.), but this is purely accidental. Syphilis is much more frequently the cause of secondary hydrocele.

THE USES OF PARAFFIN IN GENERAL PRACTICE.

By ERIC PRITCHARD, M.A., M.D., M.R.C.P.

Physician to the Queen's Hospital for Children; Physician to Out-Patients, City of London Hospital for Diseases of the Chest, Victoria Park; Honorary Physician for Infant Consultations, St. Marylebone General Dispensary, etc.

THE use of liquid paraffin, in the treatment of constipation and other conditions secondary or contributory to intestinal stasis, is now so universal in this country that it is difficult to realize that the method is comparatively new in England, and still almost unknown in foreign countries and in America. The extent to which many of us have become dependent on liquid paraffin, in the treatment of the above conditions in hospital practice, has been somewhat forcibly brought home to us by the difficulty or impossibility of prescribing it now, owing to its prohibitive price. Before the war, the price was about 4s. per gallon; at the present moment, it is about 25s.

Although the rational use of pure liquid petroleum in the treatment of constipation is quite new, crude forms of the oil, both for external and internal use, have been employed for a great number of complaints from the very earliest times. This is shown by the writings of Herodotus and Pliny, but strange as it now appears from our more accurate knowledge of its chemical and physical properties, the crude oils were chiefly esteemed as cures for bronchial and pulmonary affections, and not for their properties as intestinal lubricants.

Most of the liquid paraffins now used for internal administration are practically tasteless and free from toxic substances, but they still vary in chemical composition; indeed, the British Pharmacopœia does not fix any official standard of purity, but only insists on certain simple requirements as regards volatility and specific gravity.

Although there can be no doubt that all the liquid and solid paraffins owe their efficacy to their local and mechanical

action, it is not so very long ago that a certain largely advertised brand of petroleum emulsion obtained an immense sale as a substitute for cod liver oil. Owing to the claims that were made for it and to its superficial resemblance to Scott's Emulsion, this paraffin preparation was employed in the treatment of wasting diseases, just as if it were actually a highly nutritious food. I remember well, when I was Dr. W. B. Cheadle's House Physician at St. Mary's Hospital in 1892, that a large consignment of this emulsion was sent to the hospital, and that we tried it in the children's ward in several cases of tuberculosis with wasting. We soon gave it up, however, in favour of our old friends cod-liver oil and steel wine. Although I was unaware of the fact at the time, I subsequently learned that Dr. N. A. Randolf,[1] an American physician, had proved in the year 1884 that, if petroleum in the natural or emulsified condition was taken by the mouth, the whole of it could be recovered from the fæces, and that it had no value as a food or as a physiologically active drug. Writing on the same subject in 1899,[2] Dr. Robert Hutchison made the suggestion that paraffin might possibly serve as a substitute for mucus, in cases in which there was a deficiency of this secretion in the bowel. I am not aware that this ingenious hint was put to practical proof in the treatment of constipation before 1906, but it certainly prompted me to make the experiment in that year in a number of intractable cases of constipation in infants. I was led to make this experiment, because I was highly dissatified with the results obtained from the routine methods of treating this condition. Most of all was I dissatisfied with the results afforded by the then popular treatment of prescribing olive oil. Most physicians, who have experience in the treatment of infants, know that one of the commonest causes of constipation in artificially-fed cases is excess of fat in the food; at that time, I was less familiar with this fact than I am now.

If, in cases of constipation due to excess of fat—and the diagnosis may be made from the greasy and light-coloured character of the stools—additional supplies of fat are given in the hope of relieving the symptom, it will generally be found

[1] *Proceedings, Academy of Natural Sciences*, Philadelphia, 1884.
[2] *British Medical Journal*, March 24, 1899.

that the condition will become worse.

It is in such cases that a mechanical lubricant such as paraffin becomes indicated, and, acting on Dr. Hutchison's suggestion, I substituted it for olive oil in a number of cases with unqualified success. I have since learnt that I was not the first to recognize the advantages of paraffin in the treatment of constipation, for the late Dr. H. H. Symes-Thompson [1] wrote to the same effect in 1905, and Dr. Neville T. Wood [2] anticipated me by a few months in 1906. Moreover, the details of Professor A. Schmidt's para-regulin treatment, which embodied a similar principle, were almost simultaneously published in Germany.

The mechanical effects of paraffin as a lubricant, and the controlling influence which it exercises on intestinal stasis, explain, I believe, the high repute in which petroleum is held in the treatment of cases of chronic bronchitis and other pathological conditions, which may be secondary to intestinal intoxication. Owing to the fact that paraffin cannot be absorbed from the intestine, it can exercise no direct therapeutic influence. I was at one time inclined to believe that the high estimation, in which petroleum emulsions were held, was due to psychological causes, or possibly to the hypophosphites which they generally contained. I have, however, now modified this view, and in those cases in which the exhibition of the emulsion proves efficacious, I believe the result is due to the relief of constipation, and to the control of intestinal intoxication. This view is strengthened by my experiences with the long-continued use of paraffin in cases of exophthalmic goitre, neurasthenia, melancholia and other nervous disorders, which may be attributed to the chronic poisoning of the nervous system with the products of intestinal putrefaction. There is no class of case in which petroleum proves so universally useful as in that well known condition in children, which is accompanied by peevishness and nervous irritability, and in which the breath is offensive, the tongue coated, and the motions foul; symptoms which may be reasonably referred to the secondary effects of intestinal intoxication.

Although I think it is impossible to dispute the good results which are obtained by the continued use of paraffin in such

[1] *Transactions Med. Soc. Lond.*, Vol. 28, p. 236. 1905.
[2] *Journal West London Med. Soc.*, Ap. 1906.

cases, it is arguable whether they are exclusively due to any special properties of this mineral oil or merely to the relief of intestinal stasis. Long before paraffin was employed for internal administration, it enjoyed a high reputation as a local application to mucous surfaces in cases of chronic catarrh. There are few practitioners, I imagine, who have not prescribed the parolein spray for chronic cases of pharyngitis, laryngitis, and rhinitis, and cannot endorse the advantages of this line of treatment; further, as a local application in cases of diphtheria the crude form of paraffin, was held, before the days of antitoxin, in high estimation as a solvent of the membrane. Whether this solvent action is to be ascribed to some volatile property of crude paraffin, which is removed in the process of refining, or to some inherent property in the fixed oil, which, consequently, may be present in the pure forms now taken internally, I am unable to say, but in the *Year Book of Treatment*, 1895 (page 1678), there appears an account of some experiments which prove that the disintegration of diphtheritic membrane takes place when agitated *in vitro* with crude paraffin. It is just possible that pure liquid paraffin, when orally administered as a laxative, may have some secondary therapeutic influence in restraining intestinal intoxication, by loosening pieces of diseased membrane, or by restoring health to the mucous membrane in some other way.

In membranous and other forms of colitis, crusts of inspissated mucus often adhere to the surface of the bowel, and by interfering with normal absorption may thus predispose to putrefaction of the bowel contents. I do not think that we can claim for petroleum any direct antiseptic properties, for it is notorious that when petroleum emulsions are made with decoctions of Irish moss they very readily become decomposed, unless some additional antiseptic, such as benzoic acid, is combined with it. On the other hand, it is possible that when petroleum is well mixed up with the food which is contained in the stomach and intestine, it may promote nutrition by interference with absorption. This sounds paradoxical, but there can be no doubt that nutrition is ultimately prejudiced in an unfavourable way by the absorption of an excess of food, and most people eat too much.

In patients, therefore, who habitually over-eat, nutrition

may be benefited, if the quantity of food assimilated is controlled; provided that the passage of the unabsorbed food is facilitated through the bowel, which is almost invariably the case under the influence of paraffin.

Although relief from constipation is the common experience of those who take petroleum regularly, it must be acknowledged that in certain exceptional cases a contrary result follows, and the bowels become even more obstinate. This unexpected result may be explained as follows. In spite of the softening and lubricating influence of the paraffin, or perhaps more correctly speaking in consequence of it, the neuro-muscular mechanism of the bowel may, when paraffin is given, miss the accustomed stimulus of the scybalous mass and fail to act.

I have met with a few instances in which "biliousness" has been complained of after taking paraffin. "Biliousness" is a term somewhat loosely employed, but although usually used to indicate sensations of nausea, it more often implies some failure of liver function in consequence of overwork, as for instance in those cases in which, owing to the over-production of toxic by-products of digestion, the oxidizing and scavenging duties of the liver are over-taxed. The taking of paraffin can only relieve the liver of work of this kind, and therefore cannot predispose to this kind of biliousness. Inasmuch as paraffin is never absorbed into the system, and cannot reach this organ by any other route, it is difficult to see how it can influence liver function; neither is it probable that it directly or indirectly stimulates the stomach or intestine and thus predisposes to sensations of nausea or vomiting. On the other hand, it is conceivable that, psychologically or by suggestion, it may sometimes lead to subjective symptoms of this kind, owing to its greasy properties, its peculiar want of taste, and to ideas associated with its familiar uses.

I find, as the result of a fairly long experience of the use of the emulsion of petroleum, that there are few conditions in infancy which are not benefited by its use, when given alone or in combination with other drugs.

I now place such reliance on petroleum, that I nearly always use it, in the emulsified form, as a vehicle for administering other drugs to infants or children. Most of the abdominal pains and

discomforts from which children suffer are ascribed to "wind," and it is highly probable that "wind" implies a spasmodic contraction of some intestinal or gastric muscle, either an entero-spasm, a spasm of some sphincter, or some form of dysperistalsis. In such conditions, a lubricant, such as paraffin, by promoting the passage of the intestinal contents tends to remove the source of the spasm.

Another condition in childhood, in which paraffin is invaluable, is that of thread-worms. Before I learnt the advantage of petroleum in this connection, I never experienced much success in the treatment of this intractable condition by the use of ordinary anthelmintics, now I feel the greatest confidence that the continued and free administration of the paraffin will effect a cure.

If we can keep the fully-developed worms and their ova *on the move*, there is small probability that the parasite will have time to pass through the successive stages which intervene between ovum and maturity ; it will be expelled from the body before it can lay its eggs. In unhealthy conditions of the mucous membrane, especially when there are crypts and irregularities on its surface, where dried or semi-inspissated mucus can accumulate, the ova find the very conditions which are necessary for incubation. With the regular administration of paraffin, collections of mucus of this kind, with contained parasites or their eggs, are swept out of the bowel. In the treatment of thread-worms, paraffin need not be used to the exclusion of other drugs, which have proved their value, but rather in conjunction with them, and, if necessary, other rational hygienic expedients may be employed as well.

METHOD OF ADMINISTRATION.

Thanks to the ingenuity of the modern pharmacist, the varieties of petroleum available for administration are without number. First of all, there is the refined liquid petroleum, flavoured or unflavoured; secondly, there are a whole series of emulsions; and, thirdly, there are solid forms which are eaten or swallowed like a bolus of jam or confection. Each of these forms has its special advantage under varying circumstances and for special conditions.

Liquid paraffin, though long included in the British Phar-

macopœia among the list of official drugs, is, as I have already stated, a mineral oil of indefinite composition. As a matter of fact, no two samples of liquid paraffin are exactly identical as regards chemical constitution nor as regards taste, and, consequently, even without any artificial flavouring or colouring, both wholesale and retail houses are able to place on the market distinctive brands, under proprietary or registered names, and some of these are sold at a higher price than is warranted by their intrinsic merits. Liquid paraffin of various quantities and of different degrees of refinement is sold under the following synonyms, which are selected at random from a very long list:—Adepsine oil, Alboline, Atoleine, Glymol, Parolein, Saxol, Internol, Chrismol, and Chrismaline.

Unless there is some special object in view, or some idiocyncrasy of taste to be humoured, I would suggest that practitioners, who prescribe liquid paraffin for their patients, should order it under the official designation of "*Petroleum liquidum purum.*" Patients who take the oil every night will find it economical to purchase it by the gallon, rather than in small quantities. After the initial prejudice against swallowing so insipid and oily a liquid has been overcome, patients seldom object to the nightly dose, but for the fastidious it is quite easy to disguise the oil with an artificial cloaking of colour and taste, so that it almost defies recognition. For those who appreciate a peppermint taste and a green colour, the addition of a little chlorophyll and a small quantity of menthol or essence of peppermint, renders the oil quite agreeable and not altogether unlike the well-known liqueur "*Crême de Menthe.*"

DOSAGE.

It is very difficult to predict in any particular case what quantity of liquid paraffin will produce the required result. The appropriate dose can best be settled by a few preliminary experiments. In the majority of cases, one to two tablespoonfuls taken before going to bed give satisfactory results. Some patients who are sensitive to the influence of paraffin find a teaspoonful sufficient, while others may require as much as 2 ozs. Infants and children require smaller doses in proportion to their age. The time which liquid paraffin takes to traverse the whole length of the intestine and produce

an action, differs very materially with different individuals. Each person must discover his own "latent period," and time the dose accordingly. Some patients with voluminous intestines and pronounced stasis have very long latent periods.

I have met with several instances in which the delay between the time at which the dose is taken, and the appearance of the oil in the stools has been as much as 48 hours. In such cases, although the patient may have an action every morning with the greatest regularity, the contents of the motion represents food which was taken 48 hours previously.

EMULSION OF PARAFFIN.

A far more elegant method of administering petroleum consists in prescribing it in the form of an emulsion. In contradistinction to pure liquid petroleum, the emulsion will mix with almost any other fluid; consequently, it is easy to flavour, and it constitutes an excellent vehicle for the administration of other drugs, whether soluble or insoluble.

The fact that pure liquid petroleum will not mix, but remains in a layer either at the top or bottom of the liquid to which it is added, in accordance with the respective specific gravities of the two bodies, must clearly render it unsuitable for administration in those cases in which it is desired to incorporate a lubricating agent with the general contents of the bowel. For instance, in the prevention of the formation of those hard scybalous masses which cause so much trouble to infants and children, especially if there is a crack or fissure of the anus, a petroleum emulsion which becomes thoroughly well mixed up with the bowel contents and forms soft homogeneous stools, is far more suitable than the plain oil, which, though it may lubricate the surface of the mass and thus expedite removal, does not necessarily prevent the formation of scybala.

The disadvantages attaching to the use of the emulsions are: firstly, that they are more expensive, and secondly, that to achieve the same results they must be given in much larger doses. As usually prepared, emulsions of petroleum do not contain more than one-third their volume of the pure oil, and consequently the dose must be three times larger. Certain

emulsions ("Semprolin" brand), however, prepared by a special process are said to contain as much as 60 per cent. of standardized petroleum; if these are used, a correspondingly smaller dose is required. But since the best results with the emulsion are not obtained with the large single dose, but with the small repeated dose, the actual quantity prescribed for a dose need not be excessive.

For infants, I usually order half to one teaspoonful after each feeding, or if they are artificially fed, the same quantity incorporated with the contents of the bottle; while for adults, one tablespoonful after each meal is usually sufficient.

In ordering petroleum emulsions, whether of the Semprolin or other brands, it is most important to take precautions that a simple emulsion is provided, to which no hypophosphites or other supplementary drugs have been added. I mention this because since petroleum emulsions have become popular in the treatment of constipation, certain well known varieties which contain comparatively large quantities of hypophosphites have been taken by unsuspecting persons in the large doses which are necessary to provide the required result. The hypophosphites are most valuable drugs, but they should not be taken in large doses or they will defeat their own objects. If each teaspoonful of emulsion contains one grain of hypophosphite, and the patient takes half an ounce three times a day, he will be taking as much as 12 grains of hypophosphite in the 24 hours—far too large a dose.

The following is the formula of the petroleum emulsion which I almost invariably employ both in hospital and private practice. It has, however, this disadvantage, that it cannot be made satisfactorily in small quantities, in fact in any quantity less than one gallon.

Paraffini liquidi P.B.	-	33·00
Acidi Benzoici.		
Glusidi	ana.	0·05
Olei Cinnamomi	-	0·10
Decoctum Chondri Crispi	ad.	100·00

This emulsion has, however, the compensatory advantage that it can be made very cheaply, since the emulsifying agent,

decoction of Irish moss, is much less expensive than the mucilages of gum, acacia, or tragacanth which are usually employed.

SOLID FORMS OF PETROLEUM.

In conclusion, I would say a few words about the now popular solid forms of paraffin which are employed in the treatment of constipation.

The ordinary white vaseline is typically a solid variety, and in purity and degree of refinement it varies quite as much as the liquid forms. From the therapeutic point of view, there can be no doubt that a tablespoonful of ordinary vaseline is quite as efficacious as the very best and most expensive variety of liquid paraffin, dressed up with all the refinements of the latest pharmaceutical methods. But it would take a bold man to swallow a tablespoonful of vaseline every night, whereas there is seldom any protest against taking a similar amount of the liquid variety.

At one hospital with which I am acquainted, vaseline has been regularly prescribed for a number of years in the treatment of hæmorrhoids and painful fissures of the arms, but I can see no reason for resorting to so inartistic a method of pharmacy, now that so many new and comparatively cheap preparations, which answer the same purpose, can be employed. Since, in consequence of the war, pure liquid petroleum has become so expensive, I have been driven to find some cheaper substitute for hospital use, and I find that a very nice confection of vaseline can be made by rubbing it up with chocolate and casein. Treated in this way it loses all resemblance to its original and suggestively disagreeable progenor, and constitutes, even at present prices, a very cheap laxative.

Among the new preparations of solid paraffin must be included that very interesting series of solid emulsions which contain some 99 per cent. of liquid paraffin in a completely jellified form. These solid paraffins look uncommonly like vaseline, but unlike vaseline they can be coloured and flavoured without losing their transparency; they represent a very interesting development of scientific pharmacy. Those who are interested in the physical properties of these very remarkable emulsions will find an account of them in the Transactions of the Chemical Society, Vol. XCI., by Mr. Spencer Umfreville

Pickering.

Another excellent preparation of paraffin in the solid form is manufactured in combination with malt, and results in a very agreeable granulated powder, not unlike ordinary sugar candy or brown sugar. It is known as Wander's Malt Extract with paraffin ; it is said to contain 50 per cent. of liquid paraffin by weight, and to be made in this country—a very desirable qualification.

As in the case of the liquid paraffin so with respect to the solid forms, it is impossible to fix any definite standard of dosage, the latter must be determined by individual experiment, but, as a rule, the equivalent of one tablespoonful of the pure oil must be taken in the 24 hours to secure a good evacuation.

NON-SUPPURATIVE FORMS OF MIDDLE-EAR DEAFNESS.*

By W. STUART-LOW, F.R.C.S.

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I PROPOSE to consider those forms of middle-ear obstruction, usually thought to be non-suppurative in origin, which are a very common cause of deafness. It will be well first to recall some features in the anatomy of the middle-ear, for this will help to show how easily obstructions can occur in a cavity of such conformation.

The bony cavity of the middle ear is a chink or excavation in the petrous portion of the temporal bone. This recess is flattened laterally, being about half an inch antero-posteriorly and somewhat over half an inch vertically, the upper part being a slight bulging space called the attic. The middle-ear space, known as the tympanum, is very narrow because of a projection outwards from its inner wall, and of an indrawing of the outer wall which is membranous, viz., the tympanic membrane. The protuberance so conspicuous on the inner wall is known as the promontory, and the width of this cavity in this portion is reduced to one-sixth of an inch by the approximation of the two walls, outer and inner. Considering that this narrow space has three small bones stretching across it from without inwards, and that in the mucous lining there are folds passing from the bones to the lateral walls and roof, it is obvious that the cavity may readily become narrowed and partially obliterated by adhesions between the lateral walls, and by thickenings of these mucous folds.

The nomenclature and classification of non-suppurative obstructive forms of middle-ear deafness are very imperfect, and an improvement in this direction is much to be desired. A simple, usual, and yet sufficiently comprehensive grouping

* Based on a Lecture delivered at the Central London Throat, Nose, and Ear Hospital.

of these various forms of tympanic deafness is :—

1. *Eustachian catarrh.*
2. *Middle-ear catarrh.*
3. *Exudative catarrh.*
4. *Oto-fibrosis.*
5. *Oto-sclerosis.*

With the exception of the last, this order indicates a gradation from most simple to severe and complicated in origin, progress, prognosis, and treatment.

1. *Eustachian catarrh.*—In Eustachian catarrh, there is chiefly an excess of mucus in the Eustachian tubes, although the tympanic cavity doubtless contains an increased amount of secretion in the majority of patients.

2. *Middle-ear catarrh.*—In middle-ear catarrh, the tympanic cavity mainly holds the excess of mucus, although the Eustachian tubes are clogged as well with more or less altered mucous secretion.

3. *Exudative catarrh.*—In exudative catarrh, the mucus has become more viscid, and has formed tags and folds gluing the tympanic membrane to the inner wall of the middle-ear, and there are bands binding the ossicles and tympanic membrane in various degrees of firmness.

4. *Oto-fibrosis.*—In oto-fibrosis, the binding bands and tags have become much more fibrous, from blood-vessels having formed in their substance, and so an actual fibrous tissue change has taken place.

5. *Oto-sclerosis.*—Oto-sclerosis is in a class by itself, for it seems to be somewhat of a specific, running a definite course, always resulting in a definite osseous change, viz., an osseous fixation of the foot of the stapes at its insertion into the fossa ovalis; it springs from some cause hitherto unfathomable, and, according to my experience, it is frequently diagonally hereditary from father to daughter and from mother to son.

I will discuss these forms of tympanic deafness in the order given :—

1. EUSTACHIAN CATARRH.

This, which might be termed the acute form of middle-ear catarrh, may occur at any age, but is conspicuously common in

the younger class of patients. The reason for this will be obvious and easily remembered, when the principal cause is known to be the presence of enlarged tonsils and, especially, of adenoids. There is very frequently as well congestive nasal obstruction, and its accompanying nasal catarrh. Such patients are very liable to attacks of naso-pharyngeal catarrh, which is mostly septic in its origin, and this induces Eustachian and middle-ear catarrh. If a culture be taken from the mucus found in excess in the Eustachian tubes, septic organisms will almost invariably be discovered, but not often of the most virulent types; therefore, strictly it is not quite correct to classify these catarrhs as non-septic in origin, but it is clinically convenient to do so. A young person more or less suddenly, often after a sore throat or a head cold, develops deafness, especially in the presence of enlarged tonsils and adenoids. Such deafness is, in the larger proportion of instances, due to Eustachian catarrh. Just as the nose feels stuffy, so the ears feel muffled; deafness is then complained of, and slight singing, humming, bubbling, or cracking sounds are heard in the ears.

The diagnosis can be clinched, and the prognosis made good by applying the proper and best treatment, viz., politzerization. One effective application will always restore the hearing, and reduce or abolish the noises; it gives the Eustachian tubes and middle ear an air bath, forcing air bubbles through the mucus and dissipating the obstruction it has been causing. This ought to be repeated daily, if no inconvenience in the way of discomfort in the ears is complained of. A little mentholized vaseline (four to ten grains to one ounce) may be inserted into the nostrils by means of a camel-hair brush, after warming the vaseline in a teaspoon which has been dipped into boiling water, and the patient should be told to sniff well afterwards; this should be repeated every three hours.

The most practical point, however, is to prevent a recurrence of the symptoms. The trouble that is the primary cause should be remedied by having the enlarged tonsils and the adenoids removed, for, if these are left, recurrence is certain. Recurrence of Eustachian and middle-ear catarrh is not only the chief cause of chronic middle-ear catarrh, but at

any moment, especially in children, there may arise the serious condition of acute septic otitis media.

2. CHRONIC MIDDLE-EAR CATARRH.

This is a very common condition, often met with as a result of neglect, as indicated in the last paragraph. It is seen most frequently in adults and the middle-aged of both sexes; it is, perhaps, the most wide-spread cause of middle-ear deafness. Here again politzerization confirms the diagnosis, decides the prognosis, and supplies the most effective treatment. Deafness of varying degree, accompanied by noises of low pitched character and varying intensity, characterizes the complaint. In the majority of instances, when politzerization has been performed, the hearing is to a great degree restored, and the noises removed or improved; if these favourable results follow inflation, the prognosis is good.

The treatment should be persevered with daily for a week, and then every three days for a fortnight. Sometimes, it will be necessary to catheterize the Eustachian tubes when collapsed, for the mucus in them has become viscid, causing the sides to adhere so much that the air pressed through by the method of politzerization is not sufficient to clear the passages, and bring about that plus-pressure in the middle ear, which is the normal condition. The injection of warm mentholized parolein into the Eustachian tubes through the catheter facilitates this process by moistening and softening. Mentholized vaseline should be inserted into the nasal passages, and the tympanic membrane which may be indrawn and fixed by adhesions should be massaged. This is done by air pressure with Siegle's speculum in the meatus, a simple and safe procedure. Very often in these cases, there is some anatomical disturbance in the nasal passages causing more or less obstruction, and it is necessary to have it removed as well as the tonsils and adenoids to facilitate aeration of the middle ear.

3. AND 4. EXUDATIVE CATARRH AND OTO-FIBROSIS.

These may be looked upon as advanced forms of middle-ear catarrh, so far as their prognosis and treatment are concerned. Here, obstructions in the middle-ear are firmer, and usually fibrous and more vascular. These bands and tags pull

in the membrana tympani, impairing its movements and those of the normally mobile malleus, incus, and stapes. The Eustachian tube is usually occluded, to a varying degree.

Politzerization may benefit the hearing, but, as a rule, only slightly, in contrast with the marked improvement resulting in many persons with chronic middle-ear catarrh. This slight improvement is one of the chief diagnostic signs in establishing the presence of these more intractable forms of middle-ear trouble, and in guarding oneself against giving too favourable a prognosis. It will be necessary here to resort to catheterization to get the full good effects of inflation of the Eustachian tubes and middle ear, although the method of politzerization is not to be neglected, since occasionally it "clears the head," and the patient feels freer and hears better after it than after the use of the catheter. It is important to ascertain that there is not much impairment of the auditory nerve before pushing this treatment in these affections.

Whether tympanic massage, vibratory massage over the mastoid, politzerization, catheterization, and inflation of warm mentholized parolein into the middle-ear are to be regularly employed, depends altogether on one obvious, but often forgotten question—Is the hearing improved after them? If not, and, especially if tinnitus is made worse, or the patient upset or depressed, it is not advisable to continue to employ them. The only hope, however, of getting permanent benefit from their employment is vigorously and regularly to go on with the treatment, thus freeing the Eustachian tubes, loosening the middle ear adhesions, and restoring the chain of ossicles with the tympanic membrane to greater resiliency.

5. OTO-SCLEROSIS.

This form of obstructive middle-ear deafness stands apart, as regards its origin, diagnosis, prognosis, and treatment. It is most frequently met with in females, and is usually stated to be most common between the ages of 20 and 35; but my experience is that it occurs as well in earlier years, for I have treated girls of 12 and 14 suffering from quite confirmed oto-sclerosis. The practitioner who has usually had such cases under his care in the first instance, must be on his guard not to class them in the more favourable category that has

just been outlined.

Three features of these cases will serve to safeguard him from this mistake. Firstly, the severity of the tinnitus, which is often what the patients originally come complaining about, stating that if it were not for the noises in the head they would hear quite well; secondly, the improved hearing in a noise, such as that encountered when one travels in an omnibus or a railway train. The question, "Do you hear better in a noise?" should always be asked, for patients suffering from nerve deafness often hear worse in a noise. Thirdly, the absence of improvement on politzerization and catheterization; when nerve deafness is present, patients are often worse after these measures.

The prognosis is unfavourable, for the deafness and noises tend to increase progressively; but absolute loss of hearing is very rare, in contrast with what is commonly the case in nerve deafness.

Local treatment such as politzerization and catheterization is of no avail, for the Eustachian tubes are usually over-patent; so there is no necessity to inflate them, and such measures may tend to aggravate the terrible tinnitus. Every effort should be directed to improve the general health, and to inculcate avoidance of worry, exhaustion, and strain. On the theory that the origin of the trouble may be toxic or rheumatic, tabloids of carbonate of guaiacol (grains 5), two or three times a day, seem to be ameliorative in abating the tinnitus, and in retarding the progress of the deafness. For the noises, a combination of the bromides with large doses of dilute hydrobromic acid is the most reliable remedy.

No operative interference with the nose or throat is, as a rule, warrantable in oto-sclerosis, since no permanent benefit is likely to be gained, and the deafness and tinnitus are liable to be aggravated as a result of such measures.

A RETROSPECT OF OTOLOGY, 1914.

By MACLEOD YEARSLEY, F.R.C.S.

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No matter of any great importance has arrived during the year under review, although the literature of otology has shown distinct progress.

In *Anatomy and Physiology*, Urban Pritchard [1] published a short account of extra maculæ found in the ampullæ of some birds, and Sturm [2] has propounded a new theory of hearing, in which he suggests that the ligamentum spirale is really a muscular structure which keeps tense the basilar membrane. Shambaugh [3] considers the semicircular canals and the function of equilibrium in an ingenious paper.

As is usual in modern otological literature, the bulk of the year's papers deal with middle ear suppuration and its complications. In *suppuration*, acute and chronic, Page [4] contributes a case of probable injury to the jugular bulb, following myringotomy in an infant ten months old; Whale [5] on otorrhœa, and Kisch [6] on danger signals in suppuration of the middle ear, are useful papers.

In relation to *mastoid complications*, McCaw,[7] insists on the need of more accurate knowledge in the diagnosis of mastoiditis by the general practitioner, and Bacon [8] discusses laboratory aids in the diagnosis of acute mastoid disease, due to acute purulent otitis media. Barnhill [9] describes two cases of sarcoma of the dura simulating mastoiditis, and Kopetzky [10] records an interesting case of latent mastoiditis, complicated by toxic and irritative cerebral symptoms, and accompanied by blindness and a streptococcæmia caused by trauma. Lake [11] discusses acute suppuration of the mastoid and its treatment; Sharp [12] describes when the radical mastoid operation is imperative, and Dighton [13] considers the mastoid operation generally. Canesteo [14] and Hammond [15] both describe interesting cases in which parotid fistulæ followed the mastoid operation; the former occurred in a boy of four, the latter

in a child of nine.

The literature of other *complications of suppuration* are best represented in three papers. One by Westmacott,[16] on oculomotor paralyses of otitic origin, is an admirable contribution to our knowledge; one by Steel[17] on a case of meningitis without definite symptoms, appearing late in mastoidectomy convalescence, which occurred in a boy of eight and was diagnosed by the laboratory findings, clinical symptoms of meningitis appearing late; and one by Imperatori,[18] describing a case of otitic meningitis due to streptococcus capsulatus, in a boy of seven.

The diagnosis of endocranial complications of suppurative labyrinthitis is considered by Braun[19]; Danziger[20] discusses diffuse serous labyrinthitis complicating acute purulent otitis media; and Welty[21] writes on the indications for the labyrinth operation.

Cavernous sinus thrombosis is represented by three papers, all dealing with cases. Pooley[22] relates one case; Braun[23] records one which complicated a suppuration of the labyrinth; and Friesner[24] describes an instance in which simultaneous bilateral thrombosis of these sinuses occurred 12 hours after a simple mastoid operation.

A temporo-sphenoidal abscess, secondary to chronic middle ear suppuration, in a boy of 14, is related by Ingersoll[25] and Perkins[26] describes a cerebellar abscess, in which the phenomena of ventricular distension were well shown, in a boy of 13.

Intracranial disease from the ear is discussed in general by Bardes.[27]

Catarrhal Middle-ear Deafness has received a certain amount of attention, but far less than it deserves. Beech[28] describes an interesting case in which non-suppurative middle-ear disease in a girl of 11 showed fistula symptoms. Re-education of the hearing, so-called, is discussed by Lake[29] and Muecke,[30] both of whom seriously discount the much vaunted powers of this form of treatment. Bryant[31] considers the use of aids to hearing and prostheses in middle-ear deafness; whilst Lutz[32] publishes a useful paper upon how the patient can help himself in cases of chronic catarrhal otitis media. By far the most valuable contributions, however, are

those in which the naso-pharynx is dealt with in connection with catarrhal deafness. Of these, the following may be selected: Wood [33] on the naso-pharynx in oto-rhinology; Wood [34] on direct treatment of the Eustachian tube, with an analysis of results in 17 cases; and Braislin's [35] further remarks on the use of silver nitrate, applied within the mouth of the Eustachian tube for the relief of tinnitus.

Three papers on *oto-sclerosis* are noteworthy: Digby's [36] note on the pathology of the condition; Fraser and Walker [37] on the clinical aspect of oto-sclerosis; and Jenkins [38] on its treatment.

Apart from the articles on labyrinthine suppuration, nothing noteworthy has appeared dealing with the *internal ear*, but Bárány [39] has described an interesting case of total deafness, associated with the symptom-complex of Bárány, in which complete restoration of hearing occurred.

School Hygiene and Deaf-mutism is represented chiefly by two papers: one by Grace Burton [40] on the deaf child and his education; and Macleod Yearsley [41] on the classification of the deaf child for educational purposes. This writer has also endeavoured to throw light on the origin of hereditary deafness by his research [42] on the question of concubitancy in cousin marriages.

The great question of the *prevention of deafness* gradually progresses, and more papers dealing therewith appear every year. In 1914, the most noteworthy publications were: Bryant [43] on the involution of the naso-pharynx and its clinical importance; Holmes [44] on the epipharynx in children; Wishard [45] on the conservation of hearing; and Macleod Yearsley,[46] on the problem of deafness and its prevention. Certain writers have, from time to time, insisted upon the grave necessity for dealing with meningitis as a fertile cause of infantile deafness and, in this connection, Black's paper [47] on prophylactic vaccination against epidemic meningitis is welcome.

In connection with prophylaxis, a short note by Jobson Horne [48] on gun deafness and its prevention, must be mentioned.

Miscellaneous.—During 1914, the Royal Commission on Venereal Diseases has held its sittings, and two of the

witnesses, Kerr Love and Macleod Yearsley, have given evidence upon the ravages of syphilis on the ear, especially in children. Stein,[49] has contributed a useful paper on syphilis of the ear. The serious war in which Europe is now plunged will doubtless result in a number of papers upon the effects of modern high explosives upon the hearing. The subject of injuries of the ear in war has already been discussed by Macleod Yearsley.[50]

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SOME PRINCIPLES OF X-RAY LOCALIZATION.

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THE X-ray localization of shot, bullets, and fragments of projectile within the living is at once the crux and the crown of X-ray diagnosis. The difficulties are not few, and at any time an unsuccessful appeal to the operation-table may lead to an adverse verdict in the post-mortem room. As a rule, the radiographer, if a medical man, has some knowledge of surgery, while the operative surgeon has little or no knowledge of X-ray photography; even to those surgeons who know it well, ordinary photography is often sadly misleading. Many surgeons, moreover, of wide experience can successfully extract bullets, or leave them alone, without X-ray pictures—and even in spite of them! It is easier, however, for the operating surgeon to learn radiography than for the radiographer to learn operative surgery. I hope, in the present paper, to interest the former in some of the problems and some of the methods of his X-ray colleague. In the art of applying radiography to surgery, as in the art of war itself, "he alone who has well thought out the art can practise it."

In the case of foreign bodies of this kind, by simple inspection of any simple X-ray picture, the presence and minimum number of foreign bodies can be determined; each complete silhouette represents at least one metallic fragment. But, owing to one of the essential ambiguities of shadow projection,[1] the relative position in the direction of projection of such a foreign body cannot be inferred directly in relation to the parts of the patient depicted; for instance, a bullet may be impacted into the shaft of a bone, or may lie between the bone and the picture plane, or between the bone and the focus tube, yet in all these cases, apart from other knowledge, the X-ray appearance of eclipse of the bone by the silhouette would be the same,—one dare hardly guess

which of the three conditions is the true one, even when the foreign body is of known shape and size. By perspective rules,[2] using certain precautions, we can accurately determine the directions in which foreign bodies lie within the patient. By means of X-ray stereoscopy (and its latest development, stereoscopic symphany[3]) there can be visualized to the observer's eyes, by means of two X-ray pictures, taken according to certain rules, the relative and even the actual position of the foreign bodies and their surroundings within the patient himself, as if the patient himself were transparent.

Unfortunately, the art of simple inspection of X-ray pictures is largely a matter of personal experience and often incommunicable. The science of perspective, as applied to X-ray pictures, is hardly known and generally misapprehended, and the numerous fallacies of X-ray stereoscopy have not yet been worked out. The case of bullets is particularly illusive when stereoscopically presented, for there is, under certain unknown conditions, a conflict of evidence, which may lead to contradictory visual judgements by different observers, often with subsequent disaster to the surgeon and his patient. It is only with X-ray localization proper, or radiographic stereometry, that we reach really firm ground in determining the *probable* position of the foreign body within the patient, with a view to the safest and readiest extraction possible.

The *direction*, in which a foreign body, considered as a point, lies in space within the patient, can be determined by means of one X-ray picture, and can be represented by one straight line; the *position* at which it lies can be determined only by two X-ray pictures, or one moving picture, at least, and can be represented by two straight lines intersecting at the foreign body. All methods of X-ray localization, therefore, involve at least one change of position of the patient or of the radiographic centre of emission of the focus tube.

The theory and practice of X-ray localization was fully worked out very early in the history of X-ray diagnosis. Recent increase in the number of patients, of medical radiographers, and of surgical operators has added little fresh, except in a few small details, to the earlier work of many pioneer radiographers in various countries. The three classical papers in English are those of Mackenzie Davidson, Professor

Barrell, and Mr. Shenton.[4] As a tribute to the first two of these, I would draw attention to my first figure 1, which in contradistinction to stereoscopy (or "visual stereometry"), I have labelled "visible stereometry."[5] Mackenzie Davidson, for the purpose of making his measurements, rendered the X-rays chiefly concerned in his method visible by means of

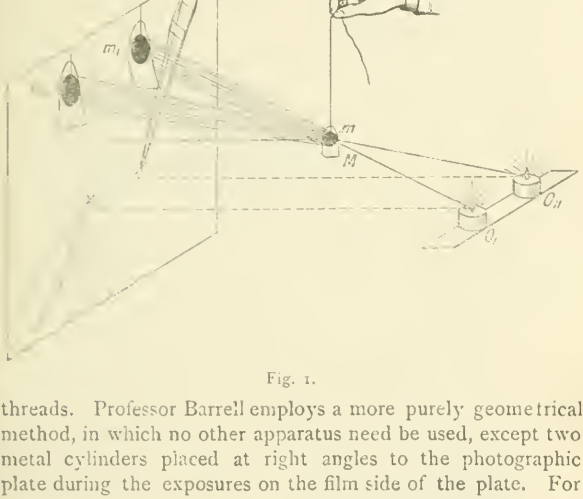

Fig. 1.

threads. Professor Barrell employs a more purely geometrical method, in which no other apparatus need be used, except two metal cylinders placed at right angles to the photographic plate during the exposures on the film side of the plate. For these cylinders, I have, in my diagram, substituted two wooden cubical blocks dusted with bismuth. Both methods involve two exposures on one plate; neither method in practice is adopted without considerable modification for use with the fluorescent screen.

By my simple method of visible shadows, many of the theorems and problems of X-ray localization can be demonstrated very simply and convincingly. Moreover, in it Mackenzie Davidson's "mouse" is rendered unnecessary, while his "monkey" is represented by a small leaden sphere (m) at the end of a string. O_I and O_{II} are the original positions of the X-ray centre of emission. M is the original

position of the foreign body to be localized, and m_I and m_{II} are the two shadows thrown respectively from O_I and O_{II}, during the original exposures to the X-rays. X_I and X_{II} are the points in the plate at which the rays, perpendicular to the plate through O_I and O_{II}, respectively cut the picture plane at the time of exposure. The distance O_I and O_{II} is called the Base; the distance X_I X_{II} upon the plate is called the base (with a small b); the distance m_I and m_{II} is called the parallax. In all that follows, unless specially mentioned, the Base is always kept parallel to the plane of the screen or photographic plate. Under this condition, the parallax in the plate is found to be always parallel to the base; and X_I X_{II} is parallel and equal to O_I O_{II}.

For X-ray localization on the screen some simple special apparatus is necessary; much elaborate or complicated apparatus is unnecessary. What is wanted is sufficient knowledge of method to be able at a pinch to improvise the further apparatus needed for localizing, in any place where it is possible to instal and work an X-ray apparatus at all, for instance, in any base hospital with all its mechanical and electrical resources.

In my next figure 2, I have drawn the essentials of such apparatus, which might be simplified even further. For instance, horizontal and vertical scales are clearly not needed, when one can get a reliable inch tape or a carpenter's folding rule; or again, a rectangular base could be improvised out of a lidless empty grocery box, into which one could put the usual three-castored base of any upright of ordinary pattern, so as not to lose the advantage of the edge of a floor plank as a straight guiding line.

The apparatus figured is of the type where the patient lies horizontally with the tube below, and the screen above him. The horizontal position is the position of muscular relaxation and repose, of general anæsthesia and surgical operation, and is, I understand, the position of the cadaver when frozen for the purpose of making topographical sections. When any X-ray examination is made with the patient more or less upright, gravitation alters the position seriously of the parts, organs, and contents from what they occupy in the lying position, and when the foreign bodies are loosely encysted or

surrounded by morbid fluid effusion, they may in the former case gravitate in a different direction, and alter their place from what they would assume in the horizontal position. More particularly, the apparatus consists of a table, an upright standard, and a plate and screen holder. Any long narrow flat table with straight sides and horizontal top will do, provided the top is quite pervious to X-rays—a level stretcher on tressels would, in certain circumstances, be very suitable. The table

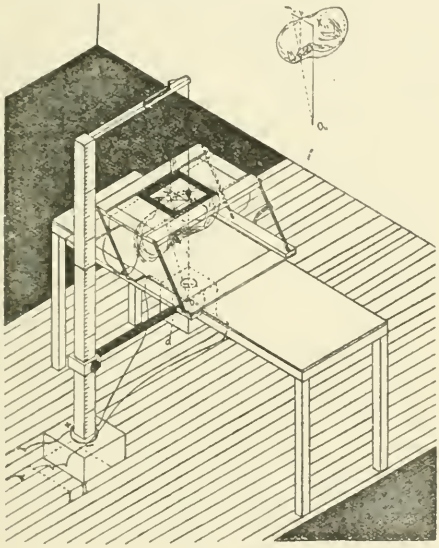

Fig. 2.

in the diagram is, in fact, a plain old-fashioned operation table. The horizontality can always be tested by a carpenter's level.

The vertical standard need not be of any particular pattern, so long as it has two horizontal brackets, each fixed to the same length or capable of equal extension or retraction—nothing about it should be too elaborate. The lower bracket is strong enough to hold the tube box below the table, and is movable

vertically ; the upper bracket is fixed above the table, but may be made removable, and from it is suspended the plumb-line and a pointed heavy plumb-bob. The plumb-line is adjusted once for all to render visible the vertical line through the centre of emission of the focus tube below the table. This is not the place to describe any of the numerous methods of fixing this all important line, or of testing its accuracy from time to time. By a simple device, the length of the plumb-line is altered by winding or unwinding the slack.

The plate or screen holder is the only part of very special construction ; it is on the principle of the parallel rulers of an ordinary drawing set, and can be clamped at any angle with the horizontal. The lower frame slides along either side of the table, and can be reversed, taken off, and replaced from either side or end of the table ; it gives no obstacle to the passage of the X-rays, and is adapted to take any part of any patient of any size, except perhaps the orbit. The upper frame or deck is always horizontal if the table is so. The whole can be folded flat for transit. The device is useful salvage from the scrap heap, where repose for ever the remains of all orthodiagraphs and other antiquities.[6] The upper deck can support horizontally, by means of an adapter, any fluorescent screen—not necessarily a very large one—or photographic plate of any size. The screen can be drawn from side to side over the patient by means of cords. Close upon the fluorescent surface of the screen is a large removable sheet of lead glass (here shown in two leaves or sections) as thin as may be consistent with opacity to X-rays, and sufficiently sand-blasted on the upper surface to take the markings of a soft lead pencil ; these marks can readily be removed from what is really a recording surface for the fluorescent screen by india-rubber or a wet cloth at any time. The lead-glass is shown covering a much more extensive area altogether than the subjacent fluorescent screen. This glass is, optically, very transparent, and hence is exceedingly useful and handy for marking the position of the shadows, when the current is on and the room darkened, and of the extremities of the base below the two positions of the plumb-bob in any case. For the idea of this graphic surface, I am indebted to that unknown benefactor of children who invented the toy glass copying

slates in vogue over 45 years ago.

Further protection can be afforded from the baleful effects of X-rays in other well-known ways; the observer need not, however, wear gloves, if sure of his glass screen.

To get the shadow of a projectile on to the screen, the affected region must be systematically explored. With even a large screen in the central position, it is remarkable how large portions of the adult chest or abdomen may escape examination. In the first instance, the plumb-bob should be brought over the centre of the segment of the trunk or limb to be examined. Then, in the case of a limb, a movement of the screen parallel to the axis of the limb should be sufficient; in the case of the trunk, the screen should be moved from one edge of the table to the other in successive transverse zones. Whenever the shadow of the foreign body comes within one or other lateral edges of the illuminated area, the movement of the screen is to be stopped. The patient should be moved as little as possible and only for a definite reason. When the shadow of the foreign body is thus trapped, the deck of the screen holder, previously free of the surface of the body, should be clamped down, where it can lie lightly against the bared skin of the patient.

With the horizontal movement of the lit up screen, the shadows thereon flow past without change of place amongst themselves. But, owing to the fact that the parts to be projected lie between the screen and the source of illumination, when the tube is moved, not only do the shadows move in an opposite direction to the movement of the tube, as indicated by the movements of the plumb-bob, but the shadows on the screen change their relative positions. Thus, for example, the shadow of what is taken to be one foreign body may resolve itself into two shadows or more. Moreover, when the foreign body in question is near the plate, its shadow moves little if at all, and the further the foreign body and other parts depicted are from the screen the more the shadows move along the screen. The shadows of parts at the same distance from the screen move along at the same rate—this is the principle of one of Mr. Shenton's ingenious methods of localization. Thus, according to the rate of movement of the shadow of a foreign body being less than, equal to, or more than the rate of

movement of the shadow of the shaft of a bone, which it appears to eclipse in the same lines of projection, we may safely conclude the actual foreign body to be nearer the screen than the bone, impacted in the bone, or farther from the screen than the bone.

It is one of the advantages of the glass screen, roughened on its upper surface and largely overlapping the fluorescent screen, that the plumb-bob need not fall over the fluorescent screen at all, so long as it falls within the confines of the glass screen itself. Nor need the movement of the tube and its attendant plumb bob move parallel with the top or bottom line of either screen, though as a rule it is very convenient to do so. Except in a special case to be mentioned, it is of advantage to keep the line of the base a good distance from the line of the parallax upon the fluorescent screen.

When the shadow of the foreign body falls just within one of the lateral edges of the screen, the tube may be taken as in its first position. The position of the point of the plumb-bob may now be marked on the rough surface of the glass screen with a small cross (x) by means of a soft lead pencil. In any case, the position of the shadow should be marked, if small, with a small circle (o); if large, it should be carefully outlined with a short vertical pencil with one eye vertically above. The tube is now to be moved to its second position, that is if the shadow is to the left side of the fluorescent screen, then the tube is to be moved towards the left side of the fluorescent screen, and *vice versâ*. As regards the amount of lateral movement, it should in no case be more than sufficient to bring the shadow sensibly towards the opposite edge of the fluorescent screen; with a tube two to two and a half feet from the screen, the movement should be about three to five inches. The second shadow may then be marked similarly to the first, the electricity turned off and the light turned on; the patient should be kept still. The second position of the plumb-bob can now be marked as before, and the position of the first plumb-bob can be verified by comparison with two chalk marks on the floor (at I. and II. as in the diagram) if desired; in fact, this could be marked now for the first time. With pencil and ruler we now draw the base and parallax on the plate, and at once join each shadow to its respective end of the base,

getting a figure like an open camp stool or a more or less distorted Roman numeral ten (X). The point of intersection of the two inclined lines is called the crucial point, and is lettered *p*.

Figure 3 will now be understood easily. The foreign body always lies vertically in the line P.M. under *p*. The patient is now to be marked. We take a slack plumb-line by unwinding, and hold the point of the plumb-bob over *p*. The screen is then removed, and the plumb-bob is gently lowered upon the patient, marking the point where it touches

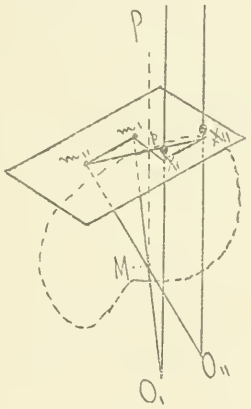

Fig. 3.

him with a small drop of strong iodine (iodized phenol leaves a mark for three or five days). The distance, if any, between the patient and the plane of the screen should be noted. When the iodine dries the patient can be removed, unless he is wanted for a photograph or stereoscopic exposure ; when a photographic plate is used, the exposure may be made in the daylight, and the position of the plumb-bob marked by a pin prick in the envelope. When the patient is to be operated on, he has only to lie in the same position on any table, with the vertical mark uppermost. In some cases, we may require to make a second mark on him vertically below the first, which can be done in many ways. The depth from M to *p* is now

determined by plotting on a vertical drawing board (or a wall as in Figure 2) either the right-angled triangle $O_I X_I m_I$ or the right-angled triangle $O_{II} X_{II} m_{II}$. O X can be known by measurement; X*m* can be taken off by compasses, as well as the position of *p* in X*m*, from the record on the rough surface of the glass screen. When a plumb-line is held over *p*, on the drawing board, etc. the required depth of M is where this plumb line cuts the line *m*O; that is, we have now directly measured the vertical depth of the bullet inside the patient beneath the iodine mark on his skin; *Q.E.F.* Plotting out can be facilitated by all sorts of ingenious devices. My own idea (borrowed, of course) is a loop of elastic cord with four drawing pins. The length *p*M can easily be calculated by the method of similar triangles; a plumb-line over *p* must often be most useful during operation.

The crucial point *p* is of great significance in the as yet incomplete theory of binocular vision. It is probably by means of something analogous to a system of crucial points, that the brain harmonizes the two dissimilar images of the external world projected on it from the two retinæ.

When the two shadows overlap and the patient is close to the screen, then the foreign body is subcutaneous on the patient's upper side. When the parallax is equal in length to the base, then the foreign body is halfway between the screen and the base, that is, probably, very near the under surface of the patient; perhaps in this case, for the surgeon generally prefers a short route of access, it would be best to turn the patient over, and localize and mark him afresh. Other interesting relations of the pencilled pattern on the glass screen I must leave to others in the meantime.

The popular plan, at present, is to run the parallax and the base into one straight line across the screen. In this case, the crucial point as such vanishes. But to avoid plotting out two sets of triangles, very ingeniously the point *m* is made to fall over *X*; so that the vertical line of projection falls along the vertical line of localization, and only one set of triangles, as in the method with the patent crucial point, needs plotting out. If anyone wishes to fish for shadow number one with the plumb-bob as a bait, he is just as likely to get a nibble with my apparatus as with any other; in doing so, a slight degree

of rotation of the vertical standard round its vertical axis would be very useful. This plan is of great advantage in the case of large and irregular shadows.

In the present state of the art of localization, naturally enough the radiographer's duty is regarded as ended when he can say "such and such a regularly or irregularly shaped bullet is to be found so many inches below such a spot on the patient." But I am not sure that something in the way of an anatomical localization might not be given, if, for instance, we had a good atlas of transverse frozen sections of the human trunk and limbs, at, perhaps, about the same level of the patient as the iodine mark on the skin, and applied the principle of proportional representation thereto,[7] allowing, of course, for pathological changes in surrounding tissues, due to the presence of a more or less irritating foreign body. We could then demonstrate visibly in the atlas the probable anatomical position of the foreign body. Clinically, foreign bodies of the kind are either regular (as small shot or intact service bullets), or irregular, namely, metallic fragments from the size of a pin's head to one square inch in the side or more. Small shot or small fragments may be radiographically dealt with, as if they were geometrically points or small spheres. But, in the case of the larger irregular fragments, as already hinted, the exact shape of which is unknown, the problem of localization while solvable gets a solution which is only approximate.

That very differently shaped opaque bodies can throw the same shadow is well known. One can by means of a candle throw the shadow of a rabbit on a bare wall, either by means of a real rabbit, or by twisting one's fingers *secundum artem*. In a more limited degree, different opaque bodies may be made to throw the same pair of shadows by two sources of illumination, as for example, under certain conditions the twin shadows of a sphere and of a disc; of a coin and of a ring; or of two hollow half spheres, with the concavity different ways.

When the foreign body is of any large size, the shadows are larger; and the parallax, if drawn, becomes a band of parallel lines, all parallel to the base. Each shadow has two poles, one remote from the base, the other nearer thereto. From one pole to the other of the shadow runs the axis of each shadow; each axis is the locus of the middle

points between the two margins of the shadow along each parallel of the parallax. The middle line of the parallax cuts the shadows at what may be called the equator of each, the middle point of this middle line is the centre of the shadow.

From the centres of the two shadows we localize not necessarily the centre of any foreign body, but what may be called its *metacentre*, namely, the centre of the space occupied but not filled by opaque bodies which with a given Base cast the same pair of shadows.

Thus, with an undistorted service bullet the surgeon would meet his foreign body rather sooner than he expected, but with a hollow fragment of any large size (concave towards the point of his knife) he would meet it rather *later*. In localizing by means of the centre of the shadow, we localize in a definite direction within the patient, at a definite depth, plus or minus an unknown quantity which may amount to half an inch or more, according as the foreign body is concave or convex to the plane of the screen. In localizing from the margins of the shadows, we may slide past the foreign body altogether ; in the case of the poles we may also miss, except in the case of a straight needle, where we may safely localize both ends.

A surgeon, however, does not reckon it a failure if he reaches his foreign body sooner than he expects ; but he does in the contrary case. My proposal simply is for the radiographer to add half-an-inch more to his calculated depth, in all cases where he localizes from the centre of the two shadows, and where probably the foreign body is large and irregular. He cannot misdirect, if he is sure of his direction ; but he may save disappointment to the surgeon due to the unknown factor of *shape*. That the surgeon in this game of hide and seek is conscious of some such source of error is indicated by his recourse to electric bell and telephone circuits, to show whether he is getting hot or cold. When the foreign body is an intact service bullet, the surgeon can safely be left to make his own allowance.

For lightly sandblasted or "satin-finished" lead glass, suitable for a recording screen, I would refer enquirers to Messrs. James Powell and Sons, Whitefriars Glass Works,

Tudor Street, Fleet Street, London, E.C. For the special screen holder, and for any modification or fitting of this, I would refer the reader to Mr. Thomas Clark, of T. Clark and Sons, 36, Falmouth Road, Bishopston, Bristol.

For want of space, I have had to omit the names of many early workers, as well as discussion of many interesting points, such as localization by movements of the patient, and vertical movements of the tube, and the nature of identifiable as distinguished from identical points, etc.

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ARTIFICIAL PNEUMOTHORAX.

By FREDERIC C. COLEY, M.D.

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My own experience, though not more favourable, I believe, than that of other workers, leads me to believe that, in suitable cases of phthisis, artificial pneumothorax is a method of treatment which has an absolutely unique value. In fact, it may effect a cure in some cases which are practically hopeless without it, not merely saving life, but making life comfortable and useful. I must be content with the briefest possible records of illustrative cases.

J. T., female, now aged 27. She first had symptoms of phthisis when she was 21. After a time, she was admitted into the sanatorium at Stannington, and remained there for 2½ years, deriving great benefit. Some time after going out, she relapsed in some degree, and was then taken into the Royal Infirmary at Newcastle-upon-Tyne, where she underwent treatment with tuberculin for four months. The result was so good, for the time, that on her discharge she believed herself to be cured. But, after a time, relapse again occurred, and she was readmitted into the Sanatorium, where she remained eight months. She gained flesh, but in other respects she was not doing so well. Her temperature was high, and the local signs showed advancing disease. On her discharge from the sanatorium, she was received into the Workhouse Hospital at Newcastle. There, by the kind invitation of Dr. Harlan, the medical officer, I had the opportunity of inducing an artificial pneumothorax. She had been about a month in the hospital when I saw her. In spite of rest in bed, her evening temperature was habitually over 100. There were signs of extensive cavity in the left upper lobe, and some crepitations in the lower lobe, but, fortunately, the right lung was fairly clear.

No difficulty was experienced in producing an efficient pneumothorax, which was done in October, 1913. Within a week, the temperature became normal, and has continued so ever since. Very gradually the cough became less, and the expectoration, which was previously purulent and copious, became thinner and diminished in quantity. When I last saw the patient, a few days ago, she told me that for some days cough and expectoration had ceased entirely. For some time, she has been feeling better and stronger than at any time since her illness began. She left

the Workhouse Hospital, at her own request, December 15, 1914. On December 22, she came to the Hospital for Diseases of the Chest, and I did a "refill," allowing her to go home the same day. Before her discharge from the Workhouse Hospital she had been allowed to give some assistance in the lighter part of the duties of a ward-maid.

A few months ago, on the side upon which the pneumothorax was done, a considerable amount of effusion was found. As in other cases, under my own observation and recorded by others, the effusion had no apparent influence on the progress of the case. In this patient, I did not draw off any of the fluid, but simply continued to inject gas above the level of the fluid from time to time; the quantity of gas was much smaller than before, in proportion as the pleural space was encroached upon by fluid. In these cases, however, it is necessary to be on the watch, lest, on the absorption of the fluid, adhesions should form and prevent the maintenance of an efficient pneumothorax.

Another very interesting case was Mrs. H. She came as an out-patient to the Hospital for Diseases of the Chest. She was only able to accomplish the journey to and from the hospital with difficulty. As there were extensive signs of cavity in the left upper lobe, and crepitations down to the left base, it was evidently useless to attempt getting her admitted into a sanatorium. The Examining Board would certainly reject her as too unpromising. I therefore took her into the hospital, and in August, 1913, induced a pneumothorax on the left side, which proved to be fairly free from adhesions. Improvement in her condition was soon apparent. After about six weeks, she was discharged from the hospital, and I continued to maintain the pneumothorax, doing the "refills" at her own house. Her strength improved so that she was able to do all her ordinary homework, except the washing and the scrubbing. The beautiful neatness of the house showed that she not only did the work, but did it energetically. One day she showed me her kitchen, which she had repapered herself. It was thoroughly well done. Then came a time, in which I had great anxiety lest all that had been done should end in disappointment. She became pregnant. Labour at term, in such a condition, seemed to involve risks which must be be quite beyond what ought to be incurred. I therefore readmitted her into the Hospital for Diseases of the Chest, and Dr. Burnett very kindly induced an abortion at about four months of pregnancy. There was a somewhat severe loss of blood, by which the patient was a good deal pulled down; but she recovered with a rapidity which was surprising, considering the circumstances.

In this patient too, effusion took place on the same side as the pneumothorax. She drew my attention to it, before the amount of the fluid was large enough to be very obvious on examination. She could feel the splash produced by making any rapid or sudden movement. Afterwards the amount of fluid increased greatly. Two or three times I drew some of it off before reinjecting nitrogen. Subsequently, when the quantity of fluid became more moderate, I simply injected gas above the level of the fluid, as required in order to keep the lung sufficiently collapsed.

On one occasion, I drew off fluid by means of the trocar

of a Potain's aspirator. But, as I always do in tapping the chest, instead of attaching the trocar to a vacuum bottle, I used simply a long tube descending to a vessel on the floor. This tube was interrupted near the cannula with a short glass tube. When gas was seen in the glass tube, it was clamped off and disconnected, and then the pneumothorax apparatus was attached to the trocar. I believe this method will be found satisfactory, when it is judged really desirable to withdraw any of the fluid, provided the hydropneumothorax is on the right side. When it is on the left side, on account of the displacement of the heart it is safer to make another puncture above the level of the fluid, and inject nitrogen simultaneously with the escape of fluid. But, as I have stated already, I believe in most cases the presence of effusion may be ignored.

I am glad to report that Mrs. H. is still doing well. A good many weeks ago, she told me that she had already passed the time to which she (and, as she had since heard, several of her acquaintances) had expected that her life would extend, when she first came to me. She not only survives, but is living a comfortable, active, and useful life. Although she is not free from cough entirely, it is slight, and there is very little expectoration.

Another very interesting case was one which I saw, by the kindness of Dr. Dickinson, at the Hospital for Infectious Diseases, Walker Gate, where a certain number of cases of phthisis are received for treatment.

N. Male. He was the subject of very advanced phthisis. On the right side, so much destruction of lung tissue, and subsequent shrinkage, had taken place that the heart was drawn over to the right side of the sternum. As a consequence, there was great tachycardia with cardiac distress. There were abundant signs of disease in all three lobes of the right lung. I determined to make the attempt to induce a pneumothorax, though, I admit, with small hope of success. I was able, however, with but little difficulty, to find space in the pleura for a very considerable volume of gas, proceeding of course very cautiously, with increasing quantities on successive days. The result was very remarkable. The heart returned to its normal site, and the tachycardia disappeared. For some months the patient did surprisingly well, and the improvement in his appearance was very striking. Then he suddenly became worse, having severe dyspnœa, and died after a few hours. Unfortunately no post-mortem was made, so that the cause of the catastrophe can only be conjectured. A rupture of a cavity in the right lung into the pleura would be not unlikely, or perhaps

an embolism in the left lung from a clot formed in the right ventricle. I believe this patient's life was prolonged for some months by the artificial pneumothorax; he was certainly made very much more comfortable. It gave a chance of recovery in a case that was otherwise hopeless.

Before concluding, I should like to make some observations on technique. The ordinary Saugman needle is open to a very serious objection. It often becomes necessary, in inducing a pneumothorax, to pass a stylet through the needle, to clear it of blood-clot, or other obstruction. Now if this is done with a Saugman's needle, when the stop-cock is opened to admit the stylet, communication is made with the external air. Then, besides the danger of sepsis from the admission of unsterilized air, there will be some risk of gas embolism, because the very fact that makes it necessary to use the stylet is a motionless manometer; and a motionless manometer is the indication that one must not admit nitrogen for fear of gas embolism. To open communication with the external air must be even more dangerous than to admit nitrogen at something less than the atmospheric pressure.

To obviate these risks, I have devised a needle with a stylet which passes through a stuffing-box, in the same way as the trocar of a Potain's aspirator. In using the needle, I do not attach the stuffing-box with the stylet in it, unless the occasion arises; but if that happens, the addition is very easily made. I have made, however, what I consider a very important improvement upon the arrangement in Potain's instrument. In that, the stuffing-box, in which the trocar works, simply plugs into the mount of the cannula. This never makes a really reliable air-tight joint. Moreover, as most of us, who have used a Potain's aspirator, know by annoying experience, the stuffing-box is very apt to tumble out at an inopportune moment. In my own instrument, the stuffing-box screws into the mount of the needle, with a washer which makes the joint absolutely air-tight. If the washer is made of india-rubber, it can be sterilized by boiling. If it is made of leather, it should be taken off, when the metal part of the instrument is boiled, and soaked in some strong solution of cresols—the substitute used for lysol. I do away with the stuffing inserted by the instrument-makers in the stuffing-box, and replace it with cotton-wool saturated with sterilized

vaseline. This is more reliable every way.

I greatly prefer this sharp needle, with a stylet and stuffing-box, for use when necessary, to Dr. Riviere's trocar and cannula described in THE PRACTITIONER for December, 1914. The object of his suggestion, viz., to avoid the risk of puncturing the lung, is very desirable. But, in my view, his instrument is not well adapted to secure that end. The method of use is, to insert the needle, with the sharp trocar, through the skin and intercostal muscles; then withdrawing the trocar, force the blunt-ended cannula through the parietal pleura. But the parietal pleura is fairly tough, and would very likely be pushed before the cannula, making a small space between the stripped-off membrane and the chest-wall. The manometric indications would closely resemble those seen when entrance is made into a very small pocket in the pleura, wholly surrounded by adhesions. There would be oscillations, but very small ones. Of course, the sharp trocar may be re-inserted, and used to perforate the parietal pleura. But then it would be far more likely to puncture the lung than a sharp-pointed hollow needle would be. Besides, a cannula with a terminal opening impinging upon the visceral pleura might easily be occluded by it. There would then be no oscillation and the operator would conclude that the lung was adherent. This would not always happen; in favourable circumstances, the lung would retract in inspiration away from the open end of the cannula. But the cannula might fail where the needle with its oblique opening would succeed, especially if the point where the puncture was made happened to be near an adhesion, though not actually the site of one.

The apparatus, shown in the figure, is one which I devised, with a view to portability and convenience, especially for use at the patient's own house. The graduated cylinder for nitrogen is of 500 c.c. capacity; *i.e.*, only half the size in ordinary use. If more than 500 c.c. are to be injected at one operation, a clip should be put on the tube leading to the needle *in situ* in the chest-wall, while the cylinder is refilled from the steel bottle of compressed nitrogen. The time occupied by this is by no means an unmixed evil. It gives the operator a better opportunity of judging whether the patient can comfortably bear the injection of more gas, and the

patient's organs more time to adapt themselves to the change produced by it.

As will be seen in the figure, the bottle is fixed on a stage which slides up and down on a brass rod, after the manner of a retort-stand. This is very convenient in use. Both the bottle and the graduated cylinder are fixed by straps, so that no packing is required. The manometer lies flat against the door of the box, and is therefore much less liable to injury than when it is about half-an-inch clear of it, as it is in other forms of the apparatus which I have seen. The door is lined with

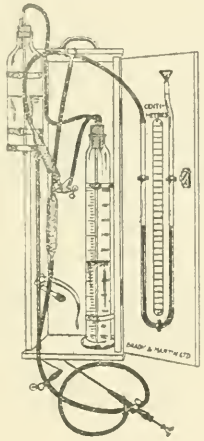

Fig. 1.

thick felt, which is a further protection for the manometer, and makes the box practically dustproof.

This apparatus is to be had, complete and ready for use, from Messrs. Brady and Martin, of Newcastle-upon-Tyne, who make as well the improved needle, which I have just described. The needle is also made by Messrs. Allen and Hanburys, of London.

During the last few months, I have been using nascent iodine (as described in THE PRACTITIONER for December, 1912, September, 1913, and June, 1914) in the treatment of a

large number of cases of phthisis. I use it in conjunction with artificial pneumothorax, as well as in cases in which adhesions are found to make pneumothorax impracticable, or when, for any reason, it is contra-indicated. When the two methods are employed together, I see reason for hoping that the nascent iodine may greatly promote the healing of any lesions existing in the comparatively sound lung, and that there may be much less risk of relapse occurring from recrudescence of activity in foci of disease left, after arrest for a time had been brought about. I have found it wise to make one modification in the method described in the articles in THE PRACTITIONER just referred to. I direct that, for the first three days, only two doses of the chlorine solution should be taken, three daily always being taken afterwards. Tolerance seems to be secured in this way, and, although I have used the method in a very large number of patients, I have never yet seen the disagreeable iodism, described as a somewhat frequent occurrence by the writers to whom I have referred. None of my patients have experienced anything more than a mere trace of coryza.

It might be anticipated that the large quantity of liquid, which has to be taken when nascent iodine is used, would destroy the appetite. This is not the case. As a rule, both appetite and digestion are greatly improved ; although there is not necessarily a corresponding increase in weight.

SOME TYPES OF PAROXYSMAL TACHYCARDIA, WITH SPECIAL REFERENCE TO THAT OF AURICULAR FIBRILLATION.

By BASIL PARSONS-SMITH, M.D.

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By the term Paroxysmal Tachycardia, we denote a morbid condition of the heart's mechanism, in which the most striking symptom, appreciable to patient and clinician alike, is an accelerated cardiac rate, or, in other words, an increased rapidity of action, paroxysmal in occurrence. With its onset, in fact, we recognize a functional upheaval of rhythm obviously and certainly prejudicial to an efficient circulation, and, in the light of modern investigation, one of extreme importance by reason of its varied ætiology.

Before proceeding, however, brief reference to the so-called functional maladies of the heart seems advisable, for it is to them that our attention now-a-days is especially directed. We endeavour to probe, as carefully as possible, the limitations of the capacities of the diseased organ, directing our inquiries chiefly towards a correct determination of the so-called functional capabilities of each individual case, to estimate the reserve power of the heart, its response to effort, and its method of action during periods of rest. Each and every case is judged upon its own merits and treated accordingly, all possible means being taken to gauge the exact value of the particular heart as a pumping machine; special consideration is naturally paid to the actual mode of life of the individual, for obviously, a lesion which may severely handicap a labourer, most certainly assumes less gravity in the rich and well-to-do classes, who do not depend for their existence on actual physical exercise.

Murmurs, if existing, must be investigated with great care, but too much weight must not be attached to their presence, for a perfectly satisfactory circulation may be maintained by

a murmuring heart, and the murmur itself itself may, quite conceivably, be of a functional character or even, possibly, pulmonary in origin. Extreme caution must, therefore, be exercised before we draw adverse conclusions from the presence of any murmur, and it is most important always to remember that a loud murmur may be produced by an insignificant lesion, and a soft murmur, heard only with difficulty, may possibly speak for gross and advanced disease; in other words, the extent of the damage cannot be estimated from any deductions based on the relative loudness or softness of a particular murmur alone. In fact, no conclusion as to the heart's efficiency is possible without a most rigid inquiry into, and an analysis of, the working capabilities of the organ, the blood-pressure it maintains, and the extent of the tone preserved by its musculature.

We may, indeed, take it as a very fair working axiom that a heart, whose muscle suffers no loss of tone at the end of an ordinary day's work, is in a highly satisfactory state of compensation, whatever the lesion present. Incidentally, it seems advisable to add, that our most valuable and reliable method of estimating cardiac tonus is by means of X-ray examinations, before and after exertion; for we know that a dilatation follows any appreciable loss of tone, and that a heart whose tonic properties are up to the normal standard, not only fails to dilate, but may even diminish in size on physical exercise, assuming the latter to be short of actual strain. Whilst, however, the condition of cardiac tonus is one of such great importance, the question of possible hypertrophy must not be overlooked; this latter entails certain pathological changes in the myocardium, an increase in the size of a large proportion of the muscle fibres, a true degeneration of others, and a varying amount of fibrous tissue deposit between the individual fibres. Consequently, cardiac hypertrophy, though essential, is not wholly beneficial, for we see that a considerable amount of degeneration accompanies the process, and with it, as we should naturally expect, comes a diminution in the heart's reserve power. We should, therefore, be quite prepared for a sudden loss of tone manifesting itself in a previously powerful hypertrophied heart, by an acute dilatation, muscular failure, circulatory embarrassment, and all the

numerous concomitant visceral stases.

For additional assistance in the diagnosis of the so-called diseases of function, which may handicap severely the heart's action, we should extend our investigations rather beyond the myocardium, in order, if possible, to obtain a clearer understanding of the mechanics of the circulation, by reviewing its facilities of action and remembering such extra-cardiac impediments as the possible presence of pericardial adhesions, an abnormally elevated diaphragmatic dome, such as occurs, for instance, with flatulent distension of the stomach or bowel, spinal curvature, and enteroptosis. Both these conditions may alter the heart's axis so as to cause kinking of the great vessels, and consequent interference with the blood stream entering and leaving the cavity of the thorax. If space permitted, it would be possible to mention numerous other factors which exert, so to speak, a harmful influence on the heart's mechanism and function; but let us return to the main object of the present paper, and discuss forthwith the clinical varieties of tachycardia in its paroxysmal form.

These may conveniently be grouped, as follows:—

A.—*Paroxysmal Tachycardia of Exophthalmic Goitre.*

B.—*Associated with Emotional States.*

C.—*Consequent on Dyspepsia.*

D.—*Of Auricular Fibrillation.*

E.—*Of Auricular Flutter.*

F.—*Dependent upon a Transposition of the Site of the Origin of the Heart's Contraction.*

A.—PAROXYSMAL TACHYCARDIA OF EXOPHTHALMIC GOITRE.

Possibly the earliest symptom, and certainly later a cardinal sign, of exophthalmic goitre is an increase in the frequency of the pulse, a constantly present acceleration persisting both with effort and repose; the condition is accounted for pathologically, partly by some lesion of the central nervous system causing a faulty and disturbed cardiac innervation, and partly by an autogenous intoxication with an excessive secretion of the thyroid gland. Whichever of these lesions, moreover, assumes the predominant influence more usually, is a point unnecessary of discussion in the present paper; the fact,

however, remains that one of the very early signs of the disease is an undue frequency of the heart beat, a rapid action varying between 90—160 or more.

At intervals, and very often following excitement, attacks of intense tachycardia supervene, which are paroxysmal in nature, and generally rapid in onset, but characterized by a very gradual return to the former rate. During the attack, the carotid arteries appear to dilate, and their pulsation becomes more than ever visible, the capillary pulsation is prominent, arterial thrills and vascular erythema appear, and the patient very rapidly reaches the stage of prostration and cardiac exhaustion.

In an endeavour to trace the ætiology of these paroxysms, we may with advantage briefly refer to the nervous apparatus of the ordinary heart. There are, as we know, the two cardiac plexuses, the superficial and the deep, both made up of branches proceeding from two great sources—(1) the vagus and (2) the sympathetic system—and both taking part in the formation of the coronary plexuses which accompany the right and left coronary arteries. Stimulation of the vagus nerve alone causes a pure cardiac inhibition, a diminished rate of beat, also incidentally a lowering of the blood-pressure and a diminished bundle conduction; whilst stimulation of the sympathetic causes an acceleration and augmentation of the beat, and improves the bundle conductively. It is extremely interesting as well to observe, amongst the numerous additional functions of the sympathetic nerve, both its pupil dilating property and its power in the causation of local sweating and flushing of the face and neck. Evidence, therefore, seems rather to point to the sympathetic control being exaggerated and having a causative relation to the paroxysms of intense tachycardia in exophthalmic goitre; for it can hardly be a coincidence that, associated with them, we invariably notice facial flushing and perspiration, increased nasal secretion, and large dilated pupils which only contract sluggishly on exposure to light.

The most important factor in treatment during the attack is quiet rest in the recumbent position, with, by way of drugs, large doses of digitalis or strophanthus combined with ammonium bromide or belladonna, the latter to soothe the

nervous system. In addition, some steps must be taken to increase the tonic activity of the vagus; of these undoubtedly the best are galvanism to the cervical portion of the nerve, or the application of a small blister, immediately behind the angle of the jaw.[2]

B.—PAROXYSMAL TACHYCARDIA ASSOCIATED WITH EMOTIONAL STATES.

Under this heading, we may very conveniently assemble the many varieties of tachycardia, which frequently attack patients whose general nervous control is in some way prejudiced; not, necessarily, by any organic malady, for the precipitating agent is most frequently some sudden fright, anxiety, fear, or other condition of emotional development. Whichever of these influences, moreover, may be the disturbing element, one notices an extreme rapidity in the sequence of cause and effect, a swift transition from normal stability to discomfort and unrest. The physical signs include a forcible apex beat, occupying an abnormally large area, and possibly accompanied by a palpable thrill; a marked increase in the rate of systole, estimated on auscultation, and reaching usually 120—160 beats per minute; the radial pulse corresponds in rapidity, but naturally shows a diminished pulse wave; venous congestion, and, in cases of a persistent character, pulmonary stasis from the venous engorgement. The symptoms include violent palpitation, oppression on the chest, and inability to breathe, with a sensation of choking, generally ascribed to the beating of the heart in the throat, as well as transient giddiness, and possibly sweating, nausea, and syncopal seizures.

The treatment of this particular form of tachycardia resolves itself into two headings:—(*a*) treatment of the paroxysm, and (*b*) treatment of the intervals.

(*a*) The first essential is rest in the recumbent position, with absolute quietude and freedom from all excitement; the cause of the attack must be ascertained and, if possible, remedied; flatulence, if persisting, will usually yield to repeated doses of sodium bicarbonate combined with carminatives, or to a few sips of warm brandy and water. The extreme discomfort is, however, most successfully relieved by the application of cold compresses to the præcordium, or

better still an icebag, combined with the internal administration of some reliable nerve sedatives, such as the bromides, chloralamide, or veronal.

(*b*) The majority of the sufferers from this particular type of tachycardia belong to the great army of neurasthenics. One's natural tendency, therefore, during the intervals of freedom from the attacks, is generally to tone up the entire system, to inquire into the patient's habits and mode of life, to prescribe regular exercise, fresh air, and, what is equally important, some definite occupation, and diligently avoid any known precursor of the attacks in question. These regulations duly observed, aided by short courses of bromide and valerian, or iron and arsenic, invariably produce a marked improvement, if not an absolute cure.

C.—PAROXYSMAL TACHYCARDIA CONSEQUENT ON DYSPEPSIA.

Among the numerous conditions recognized now-a-days as responsible for paroxysms of tachycardia, mention must be made of the particular variety associated with errors of digestion in the stomach.

The patient complains of palpitation, nausea, flatulence, and difficulty in breathing, during the attack. On examination, we find a marked fullness in the epigastrium, corresponding with an extension of gastric resonance both in the upward and downward directions. A test meal unmasks, still further, the limits of the perverted digestion, and accurately exposes the presence of several abnormal gases and acids, such as, for instance, lactic acid, butyric acid, and acetic acid, one and all the products of a fermentation process entirely foreign to a healthy stomach.

It seems, moreover, perfectly clear that a definite causal relationship becomes established between the cardiac and gastric phenomena, in which excessive fermentation and gas production assume the highest importance. The reason is that the stomach, whose functions are so disorganized, exerts an evil influence upon the heart, and, in so doing, may choose one of two possible routes:—(*a*) The *mechanical*, which depends purely upon the gaseous distension and increased pressure in the stomach, causing the superior pole of the latter to travel upwards, and thereby imposing upon the heart an

impediment the action of which is to dislocate the viscus *in toto*, and to produce a varying amount of kinking of the great vessels at its base; (*b*) The *reflex*, so called because fermentation is rife in the stomach, and, as a consequence, its mucous membrane is permanently bathed by a solution of foreign acids and poisonous mucus, to such an extent that the nerve fibrils suffer an extreme stimulation, and impulses pass from the gastric to the cardiac branches of the vagus nerve.

Accepting, therefore, the foregoing, no difficulty need be experienced in realizing that the stomach, when disorganized, may react upon the heart, interfere with its contraction, and give rise to alterations of rhythm, which mainly express themselves as bouts of tachycardia or showers of premature contractions in patients whose chief complaint may be excessive palpitation, fulness in the chest, inability to breathe, or pains of an anginal nature. In other words, to localize the origin of certain cardiac disabilities, we must focus our attention upon the stomach, and endeavour, by every possible means, to improve its functional power, realizing full well the unfortunate complications which may develop if the disease progress to any marked extent.

Naturally, success or failure in the treatment of cases under this heading depends very largely upon an appropriate employment of dietetics. The food should be plain and nutritious; the meals, by preference, taken with the smallest quantity of fluid possible; gas-producing agents,[8] such as pastry, green vegetables, sweets, and, in fact, all carbohydrates, should be cut down to a minimum, and spirits, which drift the patient towards alcoholism, are in the majority of instances not allowed. As a general rule, one should entirely forbid the use of alcohol as a beverage, especially the forms most harmful to the condition under consideration, viz., bitter ale, stout, sweet wines, and those of the sparkling variety, and, in special cases only, allow a very moderate consumption of some well-matured wine, as, for instance, a sound Burgundy or Bordeaux, the stomachic and carminative properties of which are to be relied upon. The therapeutic indications are satisfied usually by a preliminary course of bismuth and soda, with a few drops of dilute prussic acid and some aromatic carmina-

tives; this may be followed later by a bitter tonic, containing small doses of strychnine, to restore tone to the stomach wall. The more severe types, however, will require the addition of gastric disinfectants, such as carbolic acid, creosote, or sulpho-carbolate of soda, and possibly even an alkaline lavage to dissolve the excess of mucus and to neutralize the superfluous acids formed between the meals.

D.—PAROXYSMAL TACHYCARDIA OF AURICULAR FIBRILLATION.

Considerable attention has been devoted, during recent years, to the study and investigation of the signs and symptoms associated with that particular condition of the heart which has been labelled, somewhat appropriately, auricular fibrillation. This title is, moreover, suitably expressive, for, by it, we are led to suppose that the auricular chamber is in a state of fibrillation, or perpetual tremor, in contradistinction with the normal systolic contraction of the cavity. That this represents the actual state of affairs, convincing evidence is forthcoming in the shape of actual graphic records and X-ray examinations, as well as the deductions drawn from certain experiments performed on animals, and actual inspection of the heart *in situ* in several particular instances.[5]

This evidence, however, requires no elaboration here; it is quite sufficient to realize that we are dealing with a state of disordered cardiac mechanism, which represents one of the more important landmarks in the clinical history of certain patients, and which expresses itself by a variety of manifestations, such as, for instance:—

(*a*) A pulse, more often than not, rapid and irregular, but in certain instances slow and orderly in rhythm.

(*b*) A diminution in the cardiac reserve power, readily appreciable in consequence of the production of certain signs, among which mention may be made of the following:—dyspnœa, cyanosis, palpitation, œdema, faintness, nausea, vomiting, and insomnia.

(*c*) An absence of the normal venous *a* wave, and of the normal *P* wave on the electrocardiogram; a sure proof that the auricular contraction is in abeyance.

(*d*) Minute oscillations on the electrocardiographic record,

best defined during the diastolic phase, which result from the auricular tremor; the latter completely submerges the sino-auricular impulses, and supplies an irregular series of stimuli which descend to activate the ventricle.

(*e*) Paroxysmal attacks, from time to time, of extreme tachycardia, so very intense as to upset temporarily the circulatory balance, and rapidly evoke the signs and symptoms of distress; such paroxysms represent merely a phase in the evolutionary progress of auricular fibrillation, but they seem worthy of special attention in certain instances, as, for example, in the matter of the patient whose clinical notes are briefly appended.

Mr. B., aged 73, had passed through the usual childish complaints, but denies rheumatism, diphtheria, scarlet fever, throat affections and any form of venereal disease. During the past seven years, patient has suffered continuously from heart trouble and frequent attacks of acute dilatation, in consequence of which all exertion has perforce been abandoned and an evenly regulated sedentary existence enjoined; the latter proved eminently successful, and, except for an occasional attack, nothing noteworthy occurred until the early part of 1912, when the heart suddenly assumed the rhythm of auricular fibrillation, and the circulation, previously somewhat feeble, became further impeded.

With treatment, however, which, in the main, consisted of rest in bed and small doses of digitalis, the condition was kept under control, and the malady remained one of signs rather than symptoms, probably because the patient realized his state and the limitations of his disease.

On November 6th, 1913, patient was suddenly seized with an attack of præcordial pain and extreme palpitation, with sickness, nausea, and great shortness of breath.

On physical examination, he was noticed to be in great distress, unable to lie down, was propped up with pillows, and breathing was laboured, 60 per minute; the mucous membranes and the finger tips were cyanosed; the tongue was coated but moist; the pupils normal in size, equal and active; the conjunctivæ presented a slight yellow tinge. The lungs were resonant to percussion, and the air entry was everywhere quite good, except at the bases posteriorly, where signs of stasis were very evident. The apex beat of the heart was seen and felt to be very diffuse, the maximum impulse being situated in the 6th space 14·5 cm. from the median line; the right border of cardiac dulness was at the right border of the sternum, the left border extended from the apex upwards as far as the 3rd interspace, 6 cms. from the median line; no thrill was felt. The sounds at the apex were faint and disorderly, those at the base accentuated, that at the aortic area being the louder; no murmur was audible. The radial pulses were small, extremely irregular, easily compressible, and not possible to count. The liver was enlarged, and could be felt three fingers' breadth below the costal margin; its edge was tender, as was as well the entire

epigastrium; the spleen was not felt; there was no evidence of ascitic fluid, and no œdema of the back or legs. Polygraphic tracings (Fig. 1) of the movements at the base of the neck and at the apex showed the

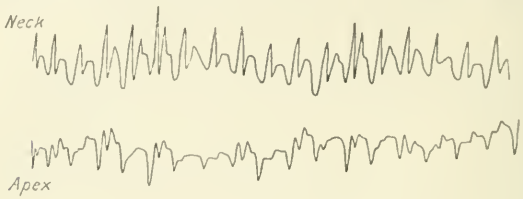

Fig. 1.

heart rate to be 188, the cardiogram clearly exposing the irregularity of the beat, and the curtailed diastolic intervals.

Digalen 1 c.c. was given intramuscularly; the pain was relieved in half-an-hour, and the patient felt decidedly more comfortable, passed a very fair night, and appeared to be much better the following morning; the breathing was less laboured, the cyanosis diminished, and the sickness had ceased; there was, however, still a feeling of flutter at the heart, and the cardiogram registered 150 beats per minute.

A second injection of digalen 1 cc. was administered, as on the previous afternoon.

The next day (November 8) patient's condition was found to be still further improved; he was able to lie comfortably in bed, breathing was easy (18 respirations per minute), and the lips and mucous membranes were no longer cyanosed; there had been no sickness, and light nourishment, including milk, broth, and jelly, had been taken without any sign of discomfort. The radial pulse had assumed a very fair volume and pressure, the individual beats, however, 82 per minute, still presenting extreme variations in size; auscultation at the apex revealed an occasional murmur, systolic in time, and an improvement in the general quality of the sounds, especially as regards the muscular element; the heart rate, counted on an apex tracing, was 96. Patient was now ordered strophanthus, ℥ x. of the tincture, six-hourly, and in two days' time (November 10) it was noted that the progress was well maintained; there were no cardiac sensations at all, in fact, the patient affirmed that he did not know that he had a heart at all; the radial pulse was easily countable at a steady, though irregular, 72. At the apex, one heard an occasional systolic murmur, seemingly only present with the more powerful systoles; at other times, the first sound was short and sharp, and the second sound inaudible; the sounds at the base were clear and, at intervals, reduplicated; the apex tracing is reproduced (Fig 2), and demonstrates, not only a lessening in the cardiac rate, 88 beats

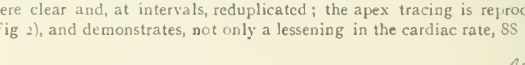

Fig. 2.

per minute, but also a lengthening of the diastolic interval, and, in spite of the irregularity of their incidence, a very fair uniformity in the size of the individual beats.

Perfectly definite grounds, therefore, seemed to exist for the assumption that the so called cardiac rest force was in process of being restored, and, to such an extent was this so during the following week, that the patient, unfortunately, decided to omit his medicine. Three days later (November 22), a very severe paroxysm of tachycardia was experienced, symptomatically more intense in nature than the previous one had been, and signalized, as before, by dyspnœa, cyanosis, an uncountable heart and pulse, vomiting, extreme prostration, etc. An attempt was made to retard the rate of the heart beat by vagal pressure; this method of treatment proved entirely unsuccessful, the probable reason being that the vagal tone was already high, and that the nerve was therefore unable to exert any further restraining influence on the heart as the result of pressure stimulation. Possibly

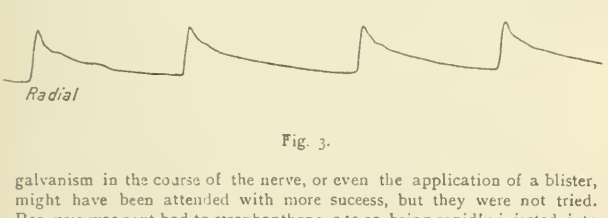

Fig. 3.

galvanism in the course of the nerve, or even the application of a blister, might have been attended with more success, but they were not tried. Recourse was next had to strophanthone, 0·5 cc. being rapidly injected into the gluteus maximus. The result was in every way satisfactory; more comfortable that evening, patient had entirely lost all his symptoms by the following morning (November 23). The pulse had assumed a very fair quality and volume, and beat steadily at 42 to the minute; the apex beat, which exhibited a coupled rhythm (Fig. 3) was counted at 84; it is, moreover, clearly seen, by reference to the tracing (Fig. 3) that the second beat of each couple fails to be represented on the radiogram, and one is tempted to suggest that the ineffectual or frustrane ventricular systole is, in each case, a premature contraction depending for its origin on the previous systole.

On auscultation, the double beat was clearly heard at the apex, the second beat, however, in each case being only represented by one sound, suggesting that the aortic and pulmonary valves were being opened only once in every two ventricular systoles, and that such was the case was proved undoubtedly by the radial pulse tracing, and also by auscultation at the cardiac base, where one clearly heard the aortic second sound coming through at a rate of 42 to the minute.

In conclusion, it should certainly be added that the coupled heart action gave rise to no uncomfortable symptoms, in fact, was accompanied

by an extraordinary sense of well-being. Cardiac coupling is quite an uncommon result of strophanthus medication, and with reference to this latter statement, it may be added that Agassiz found the phenomenon in only one of his cases, and Linnell[2] reported its occurrence in three of his series.

The further treatment of this case was uneventful; one felt that the strophanthus should be continued, and decided that the best method of administration would be a large dose bi-weekly. Accordingly, the patient was ordered ♏ xxx. of the physiologically standardized tincture, to be taken twice weekly. This method of treatment has been perfectly satisfactory, and at the time of writing patient seems better than he has been for some months past.

For all practical purposes, the treatment of the paroxysmal tachycardia associated with auricular fibrillation resolves itself into two headings: (*a*) During the attack:—Absolute rest in bed is essential, with the application of an ice bag to the præcordium and an attempt to slow down the heart by firm pressure in the course of vagus nerve. Further, one should administer a carminative if necessary, and some member of the digitalis series, either a very large dose by the mouth or bowels, or preferably by hypodermic, intramuscular, or intravenous injection; the last, naturally, produces its result most swiftly, but whichever method is adopted, the ultimate result is the same, a rapid slowing of the heart, produced either by a direct action on the auriculo-ventricular bundle, or an actual lessening of the excitability of the ventricular receptive fibres.[1]

(*b*) During the intervals of freedom from attacks:—A carefully regulated and sufficiently quiet mode of life without undue exercise and with entire freedom from overstrain; a light and easily digested diet, mainly lacto-vegetarian, but with some form of meat on alternate days; tea and coffee should be forbidden, and alcohol, in any of its forms, must only be taken with extreme caution; a regular and sufficient action of the bowels each day, and, unless contraindicated, some sound liver pill once a fortnight; short monthly courses of medicine from time to time, a tonic, for instance, one containing iron and arsenic, alternating with some one of the rather more specialized cardiac drugs, digitalis, strophanthus, theobromine, etc., combined, if necessary, with some vascular dilator. By these medicinal and general precautions, one hopes to maintain a very fair degree of compensation, and at the

same time to steady and strengthen the cardiac mechanism.

E.—PAROXYSMAL TACHYCARDIA OF AURICULAR FLUTTER.

Afforded due recognition but comparatively recently, the clinical condition, designated "auricular flutter," may best be defined as a phenomenon expressive of an intense disorder in the cardiac mechanism characterized by :—

(i) Extreme auricular acceleration,

(ii) A varying degree of auriculo-ventricular block,

the lower chamber contracting at a rate far less frequent than the upper.

The actual condition, therefore, may, for all practical purposes, be looked upon as combined heart-block and auricular acceleration, and, though tending to be persistent, occurs very frequently in paroxysms, the duration of which may be measured in minutes, hours, or even days ; as, for instance, the paroxysm noted in Case II. of Lewis's series,[6] which extended over a period of 10 days.

Seeing, moreover, that the tachycardial attacks are associated with disturbances in the auricle, our natural inquiry is how we may best determine their presence. Ordinary physical examination is not sufficient, and we require additional evidence such as that supplied by electro-cardiographic and venous curves ; the former are the more valuable, and may be looked upon as the key to the situation. In them we notice a rapid succession of P. (auricular) waves, especially well marked in Leads II. and III., and occurring so continuously that there is no iso-electric line between the auricular waves ; each individual wave, moreover, differs somewhat from the normal complex, and probably springing from an ectopic focus.[7] The ventricular complex presents, as a rule, no obvious abnormality beyond an occasional distortion, due to the super-imposition of a P. wave upon some part of its curve, and, in consequence of the block, a rate conspicuously less than that of the fluttering auricle.

Turning now to the venous curves, further proof of the incessant activity of the auricle becomes apparent, in the shape of a multitude of small waves, which, usually, however, only become clearly defined immediately before the ventricular

systole takes place. That these small waves represent definite auricular contractions, as opposed to fibrillation wavelets, has been proved from time to time, notably in the case reported by Hertz and Goodhart.[3] To these observers we are indebted for one of the earliest descriptions of auricular flutter; their case, one of mitral stenosis, exhibited, as a general rule, ventricular rapidity and a fast radial pulse, combined with an auricular systole whose rate, as estimated by X-ray examination and by jugular tracings, presented an extraordinary acceleration and an apparent inability to communicate its rapid beat to the lower chamber. Rather scouting the theory of blockage in the bundle, and yet endeavouring to account reasonably for the absence of relation between the contraction of the auricles and ventricles, their conclusion was that the vagal nerve endings in the auricle had become damaged beyond repair, and that the auricle, freed from nervous control, was enabled to run riot and maintain a rhythm, so rapid, that the ventricle was positively incapable of responding to it, and itself probably depended for its contraction upon stimuli from the auriculo-ventricular mode. Further proof that the vagal nerve endings in the auricle had suffered a severe injury, was furnished by the failure of vagal pressure to reduce the auricular rate, as well as by the experimental injection of atropine, which increased the ventricular rate, without affecting that of the auricle. This result is especially noteworthy, when we consider the usual action of atropine, and the particular effect of its injection in cases of complete heart-block, when an auricular acceleration takes place, but the ventricular rate is unaffected (Erlanger, Gibson, Stengel, Dock, Finkelburg).

While, however, Hertz and Goodhart preferred not to associate their case with any definite idea of heart-block, the opinion is now-a-days gaining ground that this is the invariable characteristic of so-called heart flutter. In confirmation of this assertion, it is interesting to note that one of the early cases of the disorder (viz., that reported by Jolly and Ritchie,[4] who, by the way, first introduced the term auricular flutter), presented evidence of complete heart-block even before the auricular paroxysms became established. In addition, they noted an extreme persistence of the flutter in spite of exercise,

atropine, digitalis and pressure, and included in their account a clear differentiation of the condition from fibrillar contractions of the auricle.

There seems, as yet, no possibility of a final decision whether the slower ventricular rate is due primarily to bundle blockage, or to an inability of the ventricle comfortably to keep pace with the fast contracting auricle. It does, however, appear somewhat contradictory to talk of heart-block with a ventricle beating at a rate of 100 or more per minute, and further a ventricle whose rate can be increased by suitable methods.

F.—PAROXYSMAL TACHYCARDIA DEPENDENT UPON A TRANSPOSITION OF THE SITE OF THE ORIGIN OF THE HEART'S CONTRACTION.

Our conception of the special forms of attack included under the present heading is based upon the assumption, that tachycardial outbursts may, and usually do, follow, if, for some reason, the sino-auricular node, which, in normal health, presides over the incidence of the cardiac beat, become replaced by some fresh focus of impulse formation, situated somewhere in the musculature of the auricles or ventricles, or even in the a—v connecting bundle itself. It is, however, important to remember that the abnormal focus may exist for several years before provoking a definite attack of tachycardia, and during this time evidence of its presence may be forthcoming by reason of an occasional heart irregularity; in other words, an extra systole crops up from time to time disturbing the otherwise regular rhythm. Soon the premature contractions become more frequent, and Stage III.[9] of the process makes its appearance in the shape of short runs of extra systoles. We may now expect the onset of a typical paroxysm of tachycardia, which, analysed by graphic methods, is found to consist of a sequence of ectopic beats, introduced by some form of extra systole, and terminating invariably in a long pause; the transition from the normal method of beat to that of the paroxysm, and the return later to the normal, are events of rapid and abrupt occurrence.

These, and other important features, chief among which may be included the peculiarly typical pulse curves and electrocardiographic tracings, stamp a clinical disorder, known to

Osler years back as "Heart Hurry," and very suitably designated "Heart Epilepsy" by Hirschfelder. Though mainly confined to young adults and patients of advancing years, it has certainly no respect for age,* and seems to arise whenever the cardiac irritability is exaggerated, either by excessive nervous influences, or by intrinsic cardiac lesions such as coronary ischæmia, or patches of fibrous myocarditis. With regard to the immediate agents by which an attack is precipitated, mention need only be made of those most frequently arising, such as fatigue, anxiety, sudden shock, emotion, gastric disorders, flatulence, excessive use of alcohol or tobacco, and in certain patients, whose cardiac irritability is highly exalted, even changes of position as from the recumbent to the standing posture. These, then, are but a selection of the more commonly observed ætiological factors, and must certainly not be regarded as a complete list, for the very good reason that others are met with from time to time; in fact, the tendency now-a-days is to be prepared for one of a very large variety of causes, rather than to expect any agent to be definitely specific for the actual onset of a paroxysm.

As we should expect, the attack itself is at all times associated with a series of signs and symptoms, peculiarly typical in that they stamp and isolate a variety of paroxysmal tachycardia, and with the material aid of graphic records, differentiate it satisfactorily from all other varieties of paroxysmal tachycardia. These physical signs and symptoms, moreover, will be found to assume a well-marked uniformity and similarity, be the cause of the attack where it may, in either auricle, ventricle, or the conducting strands of neuromuscular tissue. On inspection, one usually finds the patient sitting in bed, propped up with pillows, and breathing with difficulty; the lips and mucous membranes cyanotic; the face pale and anxious, moist with perspiration; the carotids visibly pulsating and the venous reservoirs engorged, imparting to the base of the neck an altogether abnormal fulness and distension. The chief complaints include intense palpitation, shortness of breath, and tingling down the arm, præcordial pain, nausea,

* The youngest case yet reported is that by Hutchison and Parkinson and was observed by them in a male child, aged 2½ years.—*Proceedings Royal Soc. of Medicine*, March, 1914, 117.

throbbing in the head, faintness, giddiness, flatulent distension, and an irritating cough. On examination, the heart's impulse is found to be diffuse and violent, and on percussion the area of cardiac dulness is increased, especially to the right, probably because the auricular cavities have become distended by reason of the universal venous stasis; on auscultation, the heart sounds are well heard, sharp and high-pitched, approximating to the condition known as embryocardia, and frequently uncountable, especially when the diastolic interval is curtailed to the greatest extent. The pulse may or may not be countable by ordinary methods; the blood pressure is low and ill-sustained; other important manifestations, such as hepatic enlargement and tenderness, albuminuria, vomiting, headache, pulmonary engorgement, cyanosis, and cerebral anæmia may one and all be looked upon as a direct sequence of the extreme venous stasis.

Obviously, a patient suffering from an acute paroxysm of sudden onset, and whose symptoms conform to the above brief clinical description, is in need of rapid and careful treatment; without delay he must be put to bed, the strictest quiet enjoined, and all disturbing elements removed. An attempt should then be made to quiet the heart's action by the employment of external methods, such as firm digital pressure in the course of the vagus nerves, the application of an icebag to the præcordium, or a blister behind the angle of the jaw. Further treatment may, however, still be necessary, and to stop an obstinate paroxysm, recourse may be had to such remedies as chloroform inhalation, heroin subcutaneously, amyl nitrite, digitalin hypodermically, or a maximum dose of strophanthus or digitalis by the mouth. Having by some one of these various methods allayed the immediate urgency of the symptoms, the best course to follow undoubtedly seems to consist in the prescription of some sound composing draught, Dover's powder, veronal, trional, or the like, and to follow this, during the next few days, with a short course of bromides and valerian, especially if the nervous system seems to be in a hyperæsthetic condition.

One must not be surprised, however, to meet, occasionally, cases of paroxysmal tachycardia for which no such careful treatment is necessary, the attack being not only cut short, but at times actually averted by some device of the patient, some peculiar posture, or movement, and we may be pre-

pared for conspicuous success following the use of an ordinary carminative draught in those who happen to be the victims of flatulent indigestion. On the other hand, obstinate varieties of the disorder are met with from time to time wholly resistant to all the normal forms of treatment, therapeutic or otherwise, and which, after a lengthy duration, may either cease spontaneously, or even progress to the closely allied condition known as fibrillation.

In conclusion, some few directions must obviously be given for the patient's observation during the intervals of freedom from paroxysms. A quiet mode of life is essential, with as much freedom from worry and anxiety as is possible; the diet should be light and easily digestible, with tea, coffee, and alcohol distinctly limited; tobacco is best avoided altogether, and if used at all, strict moderation is necessary; a regular action of the bowels should be enforced; the digestion should be carefully studied, and even the most trifling disorder rectified; complete and thorough mastication must be encouraged, and due explanation afforded the patient that the first process of digestion takes place in the mouth. From time to time, short courses of tonics will undoubtedly be indicated, and to these should be added small doses of some member of the digitalis group, if the heart exhibit any tendency in the direction of abnormal acceleration.

These, then, are some of the numerous points which arise in the treatment of paroxysmal tachycardia. They by no means embrace all the therapeutic measures at our disposal, for the condition may originate in such a variety of different ways, that an appropriate remedy may frequently be suggested solely after a careful consideration of all the underlying causative factors.

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OBSERVATIONS ON HYPERPIESIS AND ARTERIO-SCLEROSIS.

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ALTHOUGH arterio-sclerosis and high blood-pressure frequently go hand in hand, we know that a severe grade of either may exist without the other. A man may have vessels gnarled like the roots of a tree, and have a normal pulse tension or one of distinct hypotonus. A knowledge of this fact is of great use in differentiating between cerebral hæmorrhage and cerebral thrombosis—an important point on account of the different treatment of the two states. This tortuosity of the vessels may exist even in comparative youth, and without the subject having been the victim of wasting disease; he may never during his life become the possessor of a high vascular tension. But we can be more or less sure that a man with a high tension will sooner or later become arterio-sclerotic, though for long his vessels may be normal. In time, the continual irritation and strain produce vascular degeneration, with the attendant risk of cerebral hæmorrhage.

As has been said, arterio-sclerosis and high blood-pressure frequently co-exist; further, either may occur alone, each as a very distinct and separate state. In my experience, the higher grades of pressure—pressures of from 220 to 300 mm. Hg.—are not, for years at any rate, associated most commonly with those extreme grades of vascular degeneration one comes across when the vessels are gnarled, twisted, and calcareous, and when extremely prominent locomotive pulses are present.

To say that arterio-sclerosis comes on with age, as an involution process, is to express a mere truism. As Sir William Osler[1] tersely says: "Longevity is a vascular question: to a majority of men death comes primarily or secondarily through

[1] Sir William Osler: *The Principles and Practice of Medicine*, London, Appleton and Co., 1909.

this portal." It is not to this type that I desire to refer, but rather to that well-known clinical type which is concerned not with old age and senile decay, but with strong muscles, a fulness of animal life, and a robust frame.

Considering the fact that death comes to the majority of us through, literally, sheer vascular inability to cope with illness and the stagnating toxins engendered by disease, one cannot help wondering whether the matter gets as much prominence and consideration as it deserves. One wonders, too, whether the fact, that a man is as old as his arteries, always conveys to the medical mind as much as it ought. If so, then it seems reasonable that of all the phases of this protean disease the one to which we ought to pay most attention is the phase of *early* hyperpiesis and early arterio-sclerosis. When an otherwise robust man presents himself in the consulting room with vessels irreparably damaged and a blood-pressure of 250 mm. or so; when he explains that, for the last 20 years, he has worked strenuously and slept little, that he has drunk a dozen brandies and soda a day, and that he has practically lived—and lived generously—on beefsteaks and purin-laden articles of diet—one can only regret that 20 years ago he did not get the advice so necessary, that 20 years ago no pressure-reading was taken to show the insidious onset of hyperpiesis, at a time when advice and treatment would have been of avail.

I do not think too much stress can be laid on the vital importance of getting these cases *early*. Once hyperpiesis or arterio-sclerosis starts, one may be fairly sure of an onward and progressive march; and it is at this initial point that most good can be done. Even with late and advanced cases we can do much to prevent imminent peril or impending catastrophe; but let us suppose for a moment that advice had been asked 20 years earlier, when the hyperpietic state was beginning to creep slowly but surely on. What then? Simply this, that the progress of the disease in many cases might have been stayed. This may seem a strong statement, but I am convinced that many such cases can be saved, that the condition of many such an early state can be held *in statu quo*, provided the ætiological factor is not too strong, as, *e.g.*, chronic nephritis.

There is but one way of finding out whether every

middle-aged man is suffering from hyperpiesis or not, and that is by the simple expedient of employing the sphygmomanometer. Many a rough shock may be had from examining the vascular condition and estimating the blood-pressure of patients, who consult us for symptoms totally unconnected with the circulatory system. A short time ago, I was consulted by a gentleman of 60 years of age for subacute gastritis. In a routine examination his heart seemed practically normal. The apex beat was not displaced, and there did not appear to be any particular change in the aortic second sound, though the sounds were muffled and rather hard to hear on account of co-existing emphysema. The pulse was felt and—greatest of all medical snares and delusions—an attempt made to estimate the tension with the fingers. The pulse did not give one the feeling of a state of very high tension. Fortunately, an instrument was used, and the reading was 230 mm. Further investigation into the quality of the aortic second sound, the state of the vessels generally and the condition of the urine showed that this was clearly a case of subacute gastritis *secondary to chronic interstitial nephritis*. Had the blood-pressure not been taken, I think it would have been quite possible, if not easy, to have overlooked the true nature of the complaint. Thus did the sphygmomanometer save one from a horrible blunder!

To get a case early, when structural change has not occurred in the vessels, when at 40 or 45 years there is some unusual, though possibly slight, dyspnœa on mild exertion or a pressure of 10 to 30 millimetres beyond the normal—then and then only is the greatest chance of success. Then is the greatest opportunity, not necessarily of making an attempt to reduce the tension of that pulse, but of preventing a farther rise by removing the possibly obvious causes and of adopting treatment likely to be of avail. In such a patient the early raised pressure has been called forth, it seems reasonable to suppose, to maintain an adequate circulation in the various organs, and its reduction—were such possible—may be positively productive of harm; but if we can prevent that pressure from rising further, no small thing will have been accomplished.

Apart from the onset of nephritis, I think it will be admitted

that the establishment of hyperpiesis of any degree is generally a gradual process, a slow creeping up of the blood-pressure, in many cases a matter of a good many years, and dependent, doubtless, for rate of progress on the cause. When a man of 40 years of age has a pressure of 150 mm. (assuming the normal for this age to be 130–135 mm.) it does not seem enough to say that this is not an excessively high pressure, and one might even expect this pressure normally at that age. May it not equally well be—and is it not frequently—the beginning of hyperpiesis, and finally arterio-sclerosis and cerebral hæmorrhage? I do not think we can be too careful, when at this age a man shows a rise in blood-pressure, even though that rise be but slight. It may be, and often is, the beginning of the end.

As regards Ætiology, apart from the onset of nephritis the causes most commonly ascribed by text-books are syphilis, alcohol, lead, gout, and over-use of the muscles. While granting these as powerful ætiological factors, nevertheless there are many cases in which no such cause has ever existed. There must, then, be other causes, and these are, I believe, the following.

1. Habitual constipation and chronic intestinal stasis—alimentary toxæmia. Toxic in type. This group forms a large percentage.

2. Errors in diet—chiefly too liberal a dietary of butcher's meat, highly seasoned foods, condiments and spices, and purin-laden articles.

3. Over-eating—a point on which Sir William Osler lays stress as often being the sole factor.

4. The strain of modern life generally, especially if combined with prolonged worry.

5. Burning the candle at both ends. This consists of overwork, too short hours of sleep, continuous activity without rest or relaxation, and hurried meals.

6. Chronic septic states, *e.g.*, long-standing pyorrhœa, secondary infection of tuberculous sinuses. I have seen advanced arterio-sclerosis in a boy, of 14 years of age, who for years had suffered from secondarily infected tuberculous sinuses.

As may be observed, they separate themselves into two

great classes (*a*) toxæmia; (*b*) stress and strain. On the other hand, there are cases in which one can point to no single cause. Probably the explanation may lie in one of two things; either there is an undiscovered toxin at work, or there is an hereditary taint; the "tubing" is bad from the start.

An important factor is, I think, alimentary toxæmia. One cannot help feeling that many pathological vascular states are brought about by chronic intestinal intoxication. In many cases, there is absolutely no other factor, save the presence of this one in a marked degree. It seems feasible enough that the prolonged absorption of the products of intestinal bacteria run riot should cause irritation and spasm of the vascular coats, leading in time to hypertonus, hyperpiesis, and arterio-sclerosis. Many examples can be cited. In the *Annals of the Pasteur Institute* (January, 1913) Dr. Manouélian, working in Metchnikoff's laboratory, describes a series of experiments carried out by him on rabbits and monkeys. It has long been known that arterio-sclerosis may be set up in the later stages of infectious disease, and positive results have been obtained after experimental inoculation with the bacillus typhosus, staphylococcus, and an organism isolated from a case of ulcerative endocarditis. Manouélian used different strains of staphylococcus, and in rabbits 84 per cent. gave positive results of the production of atheroma—mostly of the aorta—in monkeys 83 per cent. In some cases, the atheroma was so marked as to tend to aneurysm. It is interesting to note that the most marked effects were produced by repeated injections of the weaker strains of coccus.

Here we have ample evidence of vascular degeneration produced by the continued absorption of bacterial products. It does not, therefore, seem unreasonable to suppose that a large number of cases of hypertension and sclerosis are of purely endogenous toxic origin, and that the toxin is, in possibly a large proportion, purely intestinal. I have not yet had the opportunity of observing fully enough the effect of treating these subjects with vaccines; but one might suggest, as worthy perhaps of consideration, that in these cases, in which there is no obvious ætiological factor apart from the state of the bowel, a vaccine might be tried if an examination of the intestinal flora

suggest its use. It seems feasible that, by this method of treatment, the vessels might be released from the spasm, irritation, and hypertonus, engendered by the slow and continuous absorption of toxic matter. At the same time, I think that the free use of paraffin is essential, along with the regular morning use of magnesium sulphate, and full doses of some guaiacol derivative. Experience has taught one that these auxiliary means render the bowel a much less receptive soil for the multiplication of organisms. We know the adverse effect of constipation in high pressure, and we know the excellent results often obtained from the free use of saline purges. That these purges act in part by depletion is, no doubt, true; but it seems likely, at the same time, that they act, too, by scouring out the bowel, and so ridding it of the toxic products of intestinal fermentation and decomposition, which can then no longer irritate and throw into hypertonus the vessel walls. One hopes ere long to have made more proof of the effect of vaccine therapy in these selected cases of vascular derangement, but their collection is of necessity slow.

Since writing the above, the discussion by the Royal Society of Medicine on alimentary toxæmia has been published. What one notes in reference to the subject of arterio-sclerosis is the statement by many, who are best fitted to judge, that intestinal toxæmia is a frequent source of hyperpiesis and arterio-sclerosis. From these statements by eminent authorities one cannot easily escape; they bear out what one has invariably found, viz., that when the bowel is thoroughly washed through daily, and that when by various means intestinal putrefaction is checked, and the absorption of alimentary toxins prevented, almost from that moment improvement takes place. The blood-pressure falls—often 30, 40, or even 60 millimetres—there is a greater sense of lightness and buoyancy produced, breathing becomes easier; in short, there is produced a feeling of well-being and a sense of rejuvenation.

I have already laid stress on the necessity of getting these cases early. There are early symptoms which lead one to suspect vascular trouble—symptoms which should lead one to make more than a cursory examination of the radials and to take exact estimations of the pressure. It may here be mentioned that arterio-sclerosis may be a purely localized

disease. I have seen the retinal vessels markedly sclerosed—typical "copper wire" arteries—without a single sign of generalized disease.

The first symptom is, when one notices a slight degree of *shortness of breath* on an amount of exertion, which ought not to cause the slightest dyspnœa. In my experience, I have never come across a case of raised arterial pressure, which did not show an unnatural tendency to shortness of breath. Though this tendency may be slight, it is invariably present in some degree. A man of about 40 to 50, apparently robust, and not over stout, who has never had rheumatism nor chorea, and who is otherwise symptomless, finds on slight exertion that his "wind" is not nearly so good as it used to be 10 years ago, and that even slight things—*e.g.*, stooping to tie a bootlace—cause distinct shortness of breath. In most cases, I venture to say that this is one of the most suspicious of all signs of raised pressure, and it gives one the hint, in spite of normal cardiac dulness and possibly unaltered cardiac sounds, to go closely into the matter of the blood-pressure, the vessels generally, and specially the aorta. Were this investigation more carefully made a matter of routine, one would see fewer cases of dyspnœa from high arterial tension labelled as "weak hearts"—a mill stone round many a patient's neck. These hearts as a rule are particularly strong. Langdon Brown[1] quotes Allbutt's protestation "against the accusation of these striving hearts of complicity in the arterial disease. . . . They are stout and faithful to the end."

Another often early sign is *headache or a sense of pressure or fulness* in the head. It is unnecessary to go into this more fully—it is already so well known—but in a young and evidently healthy man complaining of headaches, I do not know that one would naturally go first for his vascular system. Yet such conditions not infrequently exist in comparative youth. Hence the importance of being on one's guard, and the importance of invariably estimating the blood-pressure. Reputations have been made and reputations have been marred over headaches. I remember an elderly lady who was the subject of intense headaches for years. She had taken every member of the coal-tar group, almost by the pound, with no relief. She had occasion to change her

[1] W. Langdon Brown: *Physiological Principles in Treatment.*

doctor, and the new man suspected vascular trouble. From what he told me, examination showed a reading of 200 mm., some myocardial weakness, and occasional attacks of true paroxysmal tachycardia. Treatment directed to the cause completely cured the headaches, after they had persisted for several years.

Slight giddiness on assuming the erect posture quickly is another early sign. The subjects regard this as "liver." It is, in my experience, a fact, that persons suffering from arterio-sclerosis and high pressure have a very much poorer control over the splanchnic area than those with normal vessels.

Another important and often early sign is *dilatation of the venules in the malar region*. As a precursor of coming, or an indicator of existing, vascular sclerosis it is a most valuable sign. As with the facies of paralysis agitans, and as with the abdominal facies, so, too, may arterio-sclerosis have its facies.

A feeling of tightness across the chest may be another early sign, though this symptom more often belongs to the later stages, and occurring then is, I think, a useful prognostic sign, for where this is well marked the cases do not as a rule do well.

Cerebral Symptoms may be another early sign, though confined as a rule to the more advanced grades of arterio-sclerosis. A short time ago, I had the opportunity of seeing a lady, aged 50, who had never complained of anything until suddenly her left arm and leg became paretic. She had always felt well, apart from some shortness of breath. Her blood-pressure was exactly 300 mm. Hg. After 14 days' treatment it fell to 200 mm., when she was exceedingly well and free from the deep congestive flush present when the pressure was so very high, and the transient hemiplegia was present. This patient was not an arterio-sclerotic in the true sense of the word; her vessels were only very slightly thicker than they perhaps ought to have been. Here was a patient, whose vessels had not gone on to any great structural change, who had never had to consult a medical man, and whose first indication that anything vascular was wrong, was the advent of a transient hemiplegia. Had she had sclerosed vessels, one would have thought less of it.

Cough is also among the early signs calling attention to the

vascular system. It may be almost the sole thing complained of. It is often regarded as "Bronchitis," and may be either an irritating cough or a "spurious" bronchitis. The usual bronchitic remedies have little or no effect upon this vascular cough. It is surprising how it will sometimes vanish, often after having persisted for long, when the circulatory system is regulated. Due to a turgescent state of the bronchial mucosa, rest and the saline aperients and an occasional course of nitrites seem to relieve the cough more than anything else. It is sometimes puzzling to find a patient with a continual irritating cough and no localizing signs, neither in the throat, heart, nor lungs. Not infrequently the cause of it can be ascertained from the brachial artery.

Another useful sign is a sort of *sigh*, such as one meets with in cases of aortic regurgitation when dissolution is impending. Sometimes it is uninterrupted, sometimes cogwheel in type. Patients describe it as a feeling "as if there were not room enough in the chest." As these individuals are often the subjects of anoxæmia, it may be that it is a protective carbon dioxide stimulus sent to the respiratory centre. It appears to be involuntary.

Although *Insomnia* is a common feature in raised arterial pressure, one can scarcely diagnose such a condition from this symptom alone ; but what I have found to be a most suspicious sign is early waking in the morning. Those people wake frequently at 3, 4, or 5 a.m., and cannot sleep after. So often have I found this to be the case in a certain type, that I have come to regard it as almost pathognomonic.

Attention has been called to the fact that those cases often present a noticeable degree of *pallor*. This, I believe, is more to be found in states of true granular kidney, where the condition has existed for some time. With hyperpiesis there is an undoubted tendency to appear florid in the face, and often there is an underlying bluish tinge, especially if cardio-sclerosis coexists.

Digestive troubles are common, and the tendency seems to be towards hyperchlorhydria.

The frequent passage of large quantities of limpid urine of low specific gravity is often the symptom for which advice is sought. It is an almost invariable concomitant of general or

renal vascular derangement.

General weakness, loss of weight, claudication (the dysbasia angio-sclerotica of Erb), depression of spirits, evil forebodings, and many nervous symptoms may be complained of. Loss of memory and hesitation in speech are not uncommon. Premature contractions ("extra-systoles") occur in a considerable proportion of cases.

All these symptoms are more those which call attention to the vascular system. The more or less pathognomonic signs are almost too well known to mention—pressure readings, thickened vessels, ventricular hypertrophy, and changes in the aortic second sound.

As regards accentuated aortic second sounds, there are instances when an accentuated aortic second sound is best heard over the pulmonary area, sometimes in aortic aneurysm, for example. Medical text-books are curiously silent regarding the differentiation between a plus aortic and a plus pulmonary second sound. I believe these two sounds can be easily distinguished one from the other. Between these two sounds, when accentuated, there is a great difference in *quality*. The *timbre* is totally different. When there is more than usual pressure in the pulmonary system—as in some grades of mitral stenosis—the pulmonary valve closes with a booming, thudding sound, not unlike the first sound as heard in the mitral area in hypertrophy of the left ventricle. It does not have a "click" with it; nor is it high pitched. But with a plus aortic second sound—which is found when the pressure is over 200 mm. Hg.—the sound has a metallic *timbre*. It is short and sharp, and with at the same time a slight "clang." It is often distant and is exactly like the sound produced by dropping a small pebble into a deep well. It has a ring peculiar to itself, and frequently it is heard in the mitral area almost as distinctly as over the aortic cartilage—occasionally more distinctly; one knows the tendency of aortic sounds and bruits to downward conduction. This difference in quality is, at times, a very valuable diagnostic point, as, for instance, when the chest wall is deep antero-posteriorly, the lungs voluminous, and the other cardiac sounds indistinct or pathologically negative. In such types, it is heard almost as a small distant tinkle, and if the pressure is not high enough to account for its altered quality, its presence is strongly suggestive of

dilatation or aneurysm of the aortic arch. It is a sign which is pathognomonic of the aortic cusps closing under more than normal pressure.

TREATMENT.

Taking an average case, in which the blood-pressure is high, and the vessels have not gone on to great structural change, I have found the following general plan to give the best results. When the vessels are markedly thickened and tortuous, and prominent locomotive pulses are in evidence everywhere, many modifications have, of course, to be adopted.

First of all, an endeavour should be made to remove any known cause—muscular overstrain, alimentary toxæmia, general stress and strain, etc.

Then there is the regulation of the diet, both as regards quantity and quality. Heavy meals should be forbidden. Practically all red meat is cut off, and a lacto-vegetarian diet advised. All soups made from stock, all meat juices and meat extracts, spiced foods, curries, tomatoes, and all organs of animals (specially sweetbreads) are prohibited. The use of purin-free articles should be urged—milk (not in excess when the vessels are very calcareous)—eggs, cheese, bread, butter, and nuts. If possible alcohol is prohibited, or limited to a glass of a light wine with lunch and dinner. In the feeble, a small quantity of very dilute whiskey is, I think, permissible and advantageous. George Cheyne's thirteenth aphorism is applicable to-day as ever:—

"Every WISE man, after 50, ought to begin to lessen at least the quantity of his ALIMENT, and if he would continue free of great and dangerous distempers and preserve his senses and faculties clear to the last, he ought every seven years go on abating gradually and sensibly, and at last DESCEND out of life as he ascended into it, even into the child's diet."

The third essential—and, perhaps, most important of all—is the regulation of the bowels, the depletion of the vascular system, and the removal of toxic and effete products. I have come to the conclusion that no aperient does this so effectively as magnesium or sodium sulphate. But adequate dosage is required; if the pressure is very high, it is essential that one of these preparations be taken every morning, and that the evacuation should be of an exceedingly watery nature—a genuine catharsis. The relief of symptoms obtained from

this is generally remarkable: the malar turgescence vanishes, the breathing becomes easier, the head clearer, and the troublesome cough of high arterial tension and venous congestion ceases. From dieting and from the free use of Epsom or Glauber's salts, I have repeatedly seen the pressure fall 20, 40, and even 60 millimetres, with great relief of symptoms. If the pressure will not fall (provided always that it is necessary and advisable to attempt reduction) and there is no abatement in the symptoms, under this simple plan of a plain, non-nitrogenous, purin-free, limited dietary, and gentle purging, combined with rest and freedom from over-exertion and worry, then I think the chances are that we are dealing with granular kidneys.

Another aid to elimination is keeping the skin active by means of warm baths to which ammonia has been added, friction, etc. Regular gentle exercise, plenty of fresh air, for these patients are often the subjects of anoxæmia, possibly on account of coexisting emphysema, long hours of sleep—an efficient reducer of blood-pressure—freedom from worry, fear, and anxiety, and as far as possible an even, tranquil life devoid of strain and excitement, and free from strong emotional phases. This, I think, is the régime to be aimed at, and one which, if well carried out, has a marvellously calming influence on the circulation generally. If we fail to reduce pressure by these means, at least we may, and often can, succeed in doing what is in many cases equally important, which is, to prevent a further rise.

Although now more recognized, it cannot be too much emphasized, that to endeavour indiscriminately to reduce any and every high pressure is irrational and even dangerous, for some people require a raised pressure to get on at all. In speaking of "reducing pressure," I refer to two types: the first, in which the pressure is dangerously high (say from 230–300 mm.), and the patient in imminent danger of cerebral hæmorrhage; and the second, in which the pressure is causing symptoms calling for relief—dyspnœa, cyanosis, vertigo, headache, or secondary cardiac dilatation.

There are many other forms of treatment, such as massage and passive movements, certain forms of electricity, a course of Nauheim baths, etc. All these in suitable cases, give good

results, but they are not always convenient or available, and the same result may often be obtained by simpler methods.

As regards the specific treatment of excessive pressure—*i.e.*, acute cases—it has already been remarked, that to employ nitrites indiscriminately and in every case is to court disaster. One has to remember that these very high-pressure states are comparable to valvular lesions, in that they may be compensated or uncompensated. The very acute cases are often uncompensated. But, unless there are distinct symptoms, or the pressure is dangerously high, I do not think the employment of vasodilators is justifiable. The symptomless cases are compensated, and vasodilators are strongly contraindicated. Often the heart failure in high-pressure states is due to a sudden drop in the pressure; here, the indication is to endeavour to raise the pressure to its former level, if such be possible, by means of pituitrin and other preparations. The diagnosis as to whether the failure is due to continued high pressure, or to a sudden drop, can be made only by comparing present and previous pressure readings.

Granted that the pressure is excessively high, I have found that the following symptoms justify the use of vasodilators:—

1. Marked shortness of breath on exertion, not due to actual cardiac weakness. Vasodilators may ease the ventricle of the pressure to be overcome.
2. The "spurious" bronchitis already referred to.
3. Vertigo.
4. Congestion of the facial venules.
5. When there has been a history of transient attacks of monoplegia, hemiplegia, or aphasia.
6. Persistent headache.
7. Insomnia proceeding from high pressure.
8. The feeling of a sense of tightness or constriction across the chest.
9. The frequent occurrence of the "sigh" before mentioned.
10. When the pressure is a source of danger in any way.
11. Cardiac dilatation arising from the peripheral resistance offered by high pressure, to ease the burden of

the ventricle: provided always, that the pressure at the time remains high.

12. Anginal pains, or true angina pectoris.

As regards the vasodilators themselves, amyl nitrite and nitroglycerin are too transient in action to be of any use, except in angina. Sodium nitrite has a more lasting effect. It is best given in doses of from 2 to 5 grains, beginning with ½ grain. Erythrol tetranitrate has been shown to act for 6 hours, and gives good results. But by far the most efficacious preparation is the Tabloid Sodii Nitritis Co., suggested by Dr. Oliver. It is a combination of sodium nitrite, erythrol tetranitrate, mannitol hexanitrate, and ammonium hippurate. One or more may be given three times daily. Seven or eight grains of ammonium hippurate, three times daily, is of service, as well as a course of iodoglidine.

As regards the use of digitalis in these cases, one thing is certain; digitalis does not possess the power of raising the blood-pressure when that is already high. Dr. Price has already proved this, and it has been my invariable experience. That digitalis is a pressure-raiser, and therefore contraindicated when the pressure is high, is a fallacy which must be relegated to the limbo of medical myths. It is on a par with the doctrine, not so long since taught, that morphia must never be given when the kidneys are diseased; whereas it will often stop the dangerous convulsions of uræmia instantaneously, and tide an otherwise hopeless case into the zone of safety. If, in a high pressure case, there are definite symptoms calling for the use of digitalis, there is no danger in employing that drug.

We now know that the specific action of digitalis is on the *tonicity* of the heart, and when dilatation, or auricular fibrillation is present. The failures of digitalis are, I think, to be accounted for by reason of its wrong employment, viz., in cases in which there is extensive cardio-sclerosis. Here digitalis fails, for the simple reason that there is not enough healthy ventricular muscle, much of the muscle being in a fibrotic state. The better the reaction to digitalis, the greater is the amount of healthy cardiac muscle, and *vice versâ*. Many cases of high pressure with consequent dilatation respond well to digitalis;

others fail completely, and I believe this failure to respond is due, in great part, to the absence of healthy ventricular muscle, and is not a good prognostic sign. If the dilatation is not overcome, the patient will be.

The action of digitalis is a limited one; but we now know three things. First, the absolute indication for the employment of digitalis is auricular fibrillation, with or without actual heart failure; second, digitalis has a powerful action on the tonicity of the heart, and we may, therefore, expect a good result from its use in dilatation; and, third, digitalis is indicated in weak or imperfect systole.

A few years ago, I was called urgently to see a lady of 66 years of age. She was sitting in a chair in a state of acute dyspnœa, and her face was deep purple from cyanosis. There was much general anasarca, and the pulse was 130. The heart was much dilated, with a soft systolic mitral bruit; the blood pressure was 240 mm. Hg. The cardiac failure was acute. That same day she had taken a train journey of 80 miles! 15 minims of Parke, Davis & Co.'s standardized tincture of digitalis were ordered every four hours. In four days the pulse was 64. The cyanosis had vanished, the œdema had greatly decreased, and the breathing was easy and tranquil. For six months, digitalis had to be given off and on, at the end of which time the patient was again walking out of doors. I do not know any other drug which would have done what digitalis did here, and to have withheld the drug on account of the high pressure would, I feel sure, have been fatal. All through, the pressure never rose above the original level of 240 mm. Hg.

Strophanthus in my hands has proved very disappointing.

OBSERVATIONS ON THE VALUE OF DRUGS AS BLOOD-PRESSURE ELEVATORS.

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THE investigations recorded here were made to determine the effect that certain drugs, commonly supposed to act as blood-pressure elevators, have on the systolic and diastolic pressure of healthy individuals. The observations were limited to the immediate effect of the drugs experimented with, for one object of the research was to endeavour to compare their values as possible remedies for combating dangerous hypotension.

Many drugs are said to have a pressor action, simply because they cause a rise of blood-pressure when administered experimentally to laboratory animals, but it does not necessarily follow that they will have a similar effect on human subjects. My observations were made on persons with normal arterial tension rather than on patients suffering from pathological hypotension, partly because of the difficulty or impossibility in such cases of insuring with reasonable certainty that the blood-pressure of the patient remains unaffected by anything but the drug administered, but chiefly because the condition of the vessels in cases of marked hypotension has not yet been definitely determined.

Most of my observations on the effect of drugs on the blood-pressure were made on one male subject, called in this article the test subject. He was 26 years of age, in sound health, and had an average systolic and diastolic pressure of about the generally accepted normal. In a few instances, the conclusions arrived at were confirmed by observations made on other healthy individuals.

The blood-pressure readings were all taken by Korotkow's auscultatory method, the same mercurial sphygmomanometer

being used in every case. The systolic pressure was read at the beginning of the first phase of the pulsation *bruit* (the upper limit of the throb), and the diastolic pressure at the beginning of the third phase (the lower limit of the throb). All observations were made with the subjects in the sitting posture, the sphygmomanometer armlet being applied to the left upper arm at the heart level.

Before investigating the effect of any drugs on the test subject, numerous observations were made on his blood-pressure to ascertain in what circumstances it could be maintained at the most approximately uniform level. His average systolic pressure was found to be about 125 mm. Hg.; the highest systolic pressure observed was 146 mm. Hg., and the lowest 110 mm. Hg. His average diastolic pressure was about 64 mm. Hg.; the highest diastolic pressure observed was 76 mm. Hg., and the lowest 42 mm. Hg. There was very little difference between the average forenoon, afternoon, and evening readings. The effect of various factors, known to influence the blood-pressure transitorily, was investigated on several occasions; in every case, any effect produced was found to have passed off in less than an hour and a half. Several series of frequent observations on his blood-pressure and pulse-rate were then made, each series extending over a period of about three hours. For two hours before they began and while they were in progress, the subject endeavoured to do nothing which would be likely to affect his blood-pressure, and for about half an hour before they began, and while they were in progress, he remained seated in one room, the temperature of which was kept approximately uniform. It was found that the systolic and diastolic pressures, as a rule, varied very little, if, at the beginning of a series of observations, they corresponded fairly closely to the average pressures already noted. On the other hand, if they were abnormally high or low at the beginning of a series, they generally fell or rose to about normal in the course of half an hour or so. The pulse-rate on every occasion varied scarcely at all.

Most of the drugs used in these experiments are commonly employed in practice, and all had been obtained from firms of chemists of repute. Series of observations, one or more, were

made on the effect of the generally accepted maximum dose of each drug; observations on the effect of smaller and larger doses were made as well in most cases. The drugs were administered hypodermically, the injections being made into the right forearm. At least two days were allowed to elapse between each experiment, in order to be certain that the effect of the last dose had passed off completely before administering another.

Before a series of observations began, and while they were in progress, similar precautions to those mentioned were taken to exclude, as well as possible, anything but the drug administered from affecting the blood-pressure or pulse-rate. In order that the results obtained might be comparable, all the investigations were made under as nearly identical conditions as practicable. Before a drug was administered, blood-pressure readings were taken at intervals of an hour or so, with the object of supplying a basis for comparison, and of determining if they corresponded reasonably closely to the average readings previously ascertained. When discrepancies were at all marked, which occasionally happened, the experiment was abandoned for the time being; otherwise, the drug to be investigated was administered, and frequent observations on the blood-pressure and pulse-rate were begun forthwith. When any effect on the blood-pressure was produced, the observations were continued until this effect had passed off. When no appreciable effect was produced, the observations were continued for at least an hour. No series of observations have been recorded, in which the blood-pressure was obviously affected by some accidental occurrence while they were in progress.

In the accounts of the experiments which follow, the times given indicate, to within half a minute, the time at which the reading of the systolic pressure was taken; the diastolic pressure was read a second or two later. About a minute or so was allowed to elapse before the pulse-rate was noted, in order to avoid to some extent any slight accelerator effect, which the taking of the blood-pressure might have had on it.

ADRENALIN.

Some account has already been published in THE

PRACTITIONER* of observations, made on another occasion, on the effect of hypodermic injections of adrenalin upon the test subject and two other healthy male subjects. The preparation used was the 1 in 1,000 solution of adrenalin chloride, made by Parke, Davis & Co., and 10 mins. of this solution were administered.

It was found to act very rapidly on both the systolic and diastolic pressures; a marked elevation of the former occurred, and an even more marked depression of the latter. It caused as well faintness, tremulousness, palpitation, and abnormally deep respirations. The suggestion was made that the effect of the adrenalin might be due to the production of a temporary aortic regurgitation.

These observations, and others made subsequently, have led me to conclude that adrenalin is a dangerous drug, which should always be used with caution, and never as a general blood-pressure elevator.

ESERIN.

Three series of observations were made on the effect of eserin on the blood-pressure of the test subject. The preparation used was eserin salicylate U.S.P.; the effect of $\frac{1}{100}$th grain was investigated on two occasions, and the effect of $\frac{1}{50}$th grain on one occasion.

The first series of observations was made on the effect of $\frac{1}{100}$th grain of eserin salicylate. Table I. shows the effect of this dose on the blood-pressure and pulse-rate.

The systolic pressure began to rise 5–7 minutes after the drug had been administered, and remained elevated for 11–17 minutes; the highest point reached (133 mm. Hg.) was 10·5 mm. Hg. higher than the average systolic pressure observed before the experiment began. The diastolic pressure began to rise in 2–5 minutes, and remained elevated for 40–47 minutes; the highest point reached (80 mm. Hg.) was 15·5 mm. Hg. higher than the average diastolic pressure observed before the experiment began.

A sensation of nausea was first noticeable in about 25 minutes. It got gradually worse, and sweating and a sensation of general weakness followed. Vomiting occurred about

* THE PRACTITIONER, January, 1914, pp. 94–99.

40 minutes after the drug had been administered.

TABLE I.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.	
9.45	122	63	68	
10.15	124	67	72	
10 30	121	64	72	
10.43	123	64	72	
10.46	Eserin salicylate gr. $\frac{1}{100}$		—	
10.48	124	62	76	
10.51	121	75	76	
10.53	126	77	72	
10.56	132	77	72	
11	133	77	70	
11 4	127	74	72	
11.8	125	70	70	Nausea.
11.12	124	74	72	
11.16	124	77	68	
11.20	120	80	72	
11.27	119	70	72	Vomited twice.
11.31	121	70	68	
11.35	121	62	70	
11.40	124	63	72	
11.45	123	61	72	

A second series of observations on the effect of $\frac{1}{100}$th grain of eserin salicylate was made three days after those just recorded. Table II. shows how the blood-pressure was affected in this experiment.

The height and persistence of the elevation of the systolic and diastolic pressures in this case will be seen to be very similar to those observed in the first experiment. Vomiting, on this occasion, occurred about 47 minutes after the administration of the drug.

The third series of observations was made on the effect of $\frac{1}{50}$th grain of eserin salicylate. The effect of this dose on the blood-pressure and pulse-rate is shown by Table III.

The systolic pressure began to rise 9–12 minutes after the

drug was administered, and remained elevated for about 15–20 minutes; the highest point reached (137 mm. Hg.) was 11·5 mm. Hg. higher than the average systolic pressure observed before the experiment began. It then fell considerably, and 61 minutes after the administration of the drug it was 11·5 mm. Hg. lower than the average pressure observed before the experiment was begun. After this it began to rise again, but was still somewhat low when the observations were

TABLE II.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.	
9.25	126	57	78	
9.45	127	57	80	
10.10	125	56	78	
10.27	126	57	76	
10.30	Eserin salicylate gr. $\frac{1}{10}$		—	
10.32	126	56	76	
10.35	124	56	78	
10.38	127	70	76	
10.42	134	70	76	
10.46	130	72	76	
10.50	129	69	78	
10.55	126	68	78	
11	123	70	78	Nausea.
11.5	123	70	78	
11.10	124	68	78	
11.15	126	66	76	
11.20	124	60	76	Vomited once.
11.25	125	62	78	
11.30	125	59	76	
11.35	124	60	76	
11.45	123	56	76	

discontinued 45 minutes later. The diastolic pressure began to rise in 9–12 minutes, and remained elevated for 70–80 minutes; the highest point reached (74 mm. Hg.) was 18·25 mm. Hg. higher than the average diastolic pressure observed before the experiment began. The diastolic pressure

fell considerably just before vomiting occurred, but afterwards rose again for a time.

TABLE III.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.	——
10.15	128	57	68	
10.50	125	55	68	
11.5	124	55	72	
11.22	125	56	68	
11.24	Eserin salicylate gr. $\frac{1}{10}$.			
11.26	128	56	64	
11.29	124	58	64	
11.33	124	58	68	Faintness.
11.36	130	64	64	
11.40	137	67	64	Nausea.
11.45	130	74	68	
11.50	128	74	68	
11.55	125	66	70	
12	126	60	64	Vomited several times. Bowels opened once.
12.15	120	72	60	
12.25	114	74	60	
12.45	116	64	64	
12.55	120	60	68	
1.10	122	58	68	
1.20	121	58	68	

A sensation of faintness was noted about 10 minutes after the drug had been administered; this persisted until vomiting occurred, and for a short time afterwards. Nausea and sweating came on shortly after the faintness was noted. Violent vomiting and a motion of the bowels occurred between 35 and 50 minutes after the eserin was administered; after this the improvement in the general condition was fairly rapid.

Eserin was the only drug which I found would elevate both the systolic and diastolic pressure; a transitory elevation of the former and a rather more persistent elevation of the latter were produced. The pulse-rate remained unaltered, and the force of the cardiac contraction was never appreciably increased. It caused distressing nausea, vomiting, and faintness,

and for this reason its use in cases of hypotension does not seem to be advisable.

PITUITARY EXTRACT.

Five series of observations were made on the effect of pituitary extract. The preparation used was a sterilized 20 per cent. solution. Four series of observations were made on the effect of the drug on the blood-pressure of the test subject; one series on the effect of 0·5 cc. of this solution, one series on the effect of 2 cc., and two separate series on the effect of 1 cc. One series of observations was made as well on the effect of 1 cc. on a female subject who had an abnormally low blood-pressure.

The following table shows the effect of 0·5 cc. on the blood-pressure of the test subject :—

TABLE IV.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.
8.45	126	63	74
9.5	129	62	76
9.20	127	65	72
9 36	127	64	72
9.40	Pituitary extract sol. 0·5 cc.		
9.43	129	66	72
9.45	126	68	72
9.50	129	62	78
9.55	124	60	78
10	124	62	78
10 5	117	62	76
10.10	118	62	78
10.15	110	63	78
10.20	115	62	76
10.25	124	64	76
10.30	123	65	76
10 35	124	64	76
10.40	120	65	76
10 45	124	64	76
10.50	125	62	76
11	125	64	76

The systolic pressure began to fall 20–25 minutes after the drug had been administered, and remained low for about 20 minutes. The lowest point observed (110 mm. Hg.) was reached 35 minutes after the drug had been administered, and was 17·25 mm. Hg. lower than the average systolic pressure observed before the experiment began.

The effect of 1 cc. of pituitary extract solution on the blood-pressure of the test subject is shown by the following table:—

TABLE V.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.	——
8.10	129	55	76	
8.30	128	50	74	
8.40	127	58	72	
9	129	58	72	
9.5	Pituitary extract sol. 1 cc.			
9.7	130	58	70	
9.10	129	58	72	
9.15	129	57	72	
9.20	120	55	76	
9.25	122	54	72	Bowels opened once.
9.35	120	60	72	
9.40	115	60	74	
9.45	116	62	72	
9.50	114	58	70	
9.55	116	58	72	
10	117	58	72	
10.10	116	58	72	
10.20	122	60	72	
10 30	120	58	74	
10.45	125	58	70	
11.5	128	58	74	

The systolic pressure began to fall in about 15 minutes, and remained low for about 30 minutes. The lowest point observed (114 mm. Hg.) was 14·25 mm. Hg. lower than the average systolic pressure observed before the experiment began. A

motion of the bowels occurred about 25 minutes after the drug was administered.

A second series of observations was made on the effect of 1 cc. of pituitary solution. The following table shows the effect on the blood-pressure on this occasion:—

TABLE VI.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.	——
5.45	125	58	68	
6.5	129	60	72	
6.30	128	62	68	
6.40	129	58	72	
6.47	Pituitary extract sol. 1 cc.			
6.50	130	58	72	
6.55	129	59	72	
7	128	53	74	
7.5	128	57	72	
7.10	125	59	68	
7.15	120	58	72	Bowels opened once.
7.20	122	60	68	
7.25	116	60	70	
7.30	117	60	72	
7.35	118	60	70	
7.40	120	58	70	
7.50	124	58	68	
8	125	60	68	
8.15	127	62	68	
8.30	125	60	70	
8.45	127	60	68	

The systolic pressure began to fall about 25 minutes after the drug had been administered, and remained low for about half-an-hour. The lowest point observed (116 mm. Hg.) was reached in 38 minutes, and was 11·75 mm. Hg. lower than the average systolic pressure observed before the experiment began. A motion of the bowels occurred about half-an-hour after the drug was administered.

The effect of 2 cc. of pituitary extract solution on the

blood-pressure of the test subject was investigated on one occasion, and observations were made at frequent intervals for a period of four hours after the drug had been administered. The following table shows the effect of this dose :—

TABLE VII.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.	
8.5	125	60	72	
8.20	128	56	68	
8.40	125	56	72	
8.55	127	58	72	
8.58	Pituitary extract sol. 2 cc.			
9.1	128	58	68	
9.5	125	56	74	
9.15	125	58	68	Bowels opened once.
9.25	117	60	70	
9.35	118	58	74	
9.45	115	60	72	
9.55	114	60	70	
10.5	118	60	70	
10.15	121	58	70	
10.25	124	60	72	
10.35	122	60	68	
10.55	125	62	68	
11.15	125	62	66	
11.35	122	60	70	
11.55	125	62	70	
12.15	128	60	70	
12.35	128	58	66	
12.55	132	58	68	

The systolic pressure began to fall 20–25 minutes after the drug was administered, and remained low for about an hour. The lowest point observed (114 mm. Hg.) was reached in 57 minutes, and was 12·25 mm. Hg. lower than the average systolic pressure observed before the experiment began.

An easy motion of the bowels occurred, about 20 minutes

after the drug had been administered.

The following table shows the effect of 1 cc. pituitary extract solution on the blood-pressure and pulse-rate of M. S., a female subject, aged 36 :—

TABLE VIII.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.
7.45	94	48	80
8	98	48	80
8.15	98	52	78
8.30	93	48	78
8.37	Pituitary extract sol. 1 cc.		
8.41	95	48	82
8.45	92	53	80
8.50	95	49	80
8.55	95	49	80
9	98	47	80
9.5	97	54	76
9.10	98	49	76
9.15	99	48	78
9.20	96	48	80
9.25	98	52	80
9.30	96	48	80
9.35	94	48	78
9.40	94	50	76

When administered to the test subject, pituitary extract on each occasion caused a considerable fall of the systolic pressure, while the diastolic pressure and pulse-rate remained unaffected, and no unusual sensations were experienced, even with the largest dose. In the case of the female subject, the drug was not observed to have any appreciable effect.

According to Cow,[1] pituitary extract dilates the splanchnic vessels, although it constricts the systemic. He found that the constricting effect on the systemic vessels generally did not appear to outweigh the dilating effect on the splanchnics. His experiments suggest a possible ex-

[1] *Proceed. Roy. Soc. Med.*, 1911, Vol. IV., Pt. III., Pharm. Sect., pp. 86-89.

planation of the rather surprising effect I found the drug to have on healthy individuals. It is possible that, in cases of hypotension, the splanchnic vessels are already more or less fully dilated, and in marked cases cannot be dilated further by the drug. The action of pituitary extract on the vessels in such cases is, therefore, restricted to the systemic arteries which become constricted, and the blood-pressure consequently rises somewhat. In cases of moderate hypotension, the splanchnic vessels are probably not fully dilated, and hence can be dilated further by the drug; but the constriction of the systemic arteries may be just about sufficient to compensate for this extra dilatation, with the result that little or no change in the systolic pressure is obtained. On the other hand, in a person whose arterial tension is normal, the constriction of the systemic arteries, produced by a dose of pituitary extract, is probably insufficient to compensate for the simultaneous dilatation of the splanchnic arteries, as Cow's experiments seemed to indicate, and the systolic pressure falls. Unless this explanation is correct, I can only conclude from my observations that pituitary extract, when administered to the human subject in medicinal doses, is of no value as a blood-pressure elevator.

TYRAMINE.

Tyramine (para-hydroxyphenylethylamine) is an organic base produced by the action of certain ferments on tyrosine. It is said to be the most important active constituent of watery extracts of ergot.

Five series of observations were made on the effect of this drug on the blood-pressure of the test subject. One series was made on the effect of ·04 gram., two series on the effect of ·06 gram., and two series on the effect of ·08 gram. One series on the effect of ·06 gram. was made on another healthy male subject.

Table IX. shows the effect of ·04 gram. on the blood-pressure and pulse-rate of the test subject.

The systolic pressure was elevated 3–5 minutes after the drug had been administered. It remained elevated for 10–15 minutes. The maximum height (150 mm. Hg.) was attained in 8 minutes, and was 20·5 mm. Hg. higher than the average

systolic pressure observed before the experiment began. The diastolic pressure remained unaffected. The pulse-rate was somewhat slowed about 5 minutes after the drug had been administered, and remained so for 15–20 minutes.

TABLE IX.

Time. p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.
8.45	128	60	68
9.5	130	62	68
9.20	131	56	68
9.40	129	58	68
9.45	Tyramine ·04 gram.		
9.47	129	60	70
9.50	144	62	60
9.53	150	57	60
9.56	143	59	60
10	138	58	60
10.5	133	58	62
10.10	132	57	68
10.15	133	62	68
10.20	133	60	68
10.25	133	58	68
10.30	131	62	64
10.35	128	58	64
10.40	129	59	68
10.45	130	62	64
10.50	127	58	68

Table X. shows the effect of ·06 gram. of tyramine on the blood-pressure and pulse-rate of the test subject.

The systolic pressure was elevated about 3 minutes after the drug had been administered, and remained elevated for 12–15 minutes. The maximum height (149 mm. Hg.) was attained in 10 minutes, and was 26·5 mm. Hg. higher than the average systolic pressure observed before the experiment began. The diastolic pressure and pulse-rate were not appreciably affected.

Table XI. shows the effect of another dose of ·06 gram.

of tyramine on the blood-pressure and pulse-rate of the test subject.

The systolic pressure was considerably elevated 3 minutes after the drug had been administered, and remained high for 35–40 minutes. The maximum height (164 mm. Hg.) was attained in 13 minutes, and was 36·25 mm. Hg. higher than the average systolic pressure observed before the experiment began. The diastolic pressure was not definitely affected.

TABLE X.

Time p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.
3·5	122	62	68
3 15	121	60	66
3 35	124	64	66
3·55	123	62	70
4	Tyramine ·06 gram.		
4 3	129	64	66
4 5	145	62	66
4 10	149	60	68
4·15	130	62	64
4·20	125	62	68
4 25	124	58	68
4 30	122	62	70
4 35	123	60	68
4·40	122	60	68
4 50	124	64	66
5	124	60	66

The pulse-rate was slowed 5–8 minutes after the drug had been administered, and remained somewhat slow for 15–20 minutes.

Table XII. shows the effect of ·08 gram of tyramine on the test subject :—

The systolic pressure was considerably elevated 2 minutes after the drug had been administered, and remained elevated for about 40 minutes. The highest point (166 mm. Hg.) was reached in 15 minutes, and was 38 mm. Hg. higher than the average systolic pressure observed before the experiment began.

The diastolic pressure remained unaffected. The pulse-rate was slowed about 5 minutes after the drug was administered, and remained slow for about 20 minutes. Slight palpitation was noticed about 10 minutes after the drug had been administered, but had completely passed off 6 minutes later.

TABLE XI.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.
5.55	127	66	64
6.10	129	62	60
6.35	126	64	60
6.53	129	62	62
6.57	Tyramine ·06 gram.		
7	137	58	60
7.5	159	56	54
7.10	164	60	54
7.15	150	62	56
7.20	144	62	56
7.25	140	63	60
7.30	134	60	64
7.35	132	62	62
7.40	128	62	64
7.45	133	64	62
7.50	132	62	62
7.55	128	60	62
8	126	64	62

Table XIII. shows the effect of ·08 gram. of tyramine on the blood-pressure and pulse-rate of the test subject on another occasion.

The systolic pressure was elevated 3–5 minutes after the drug had been administered, and remained high for 45–50 minutes. The highest point (153 mm. Hg.) was reached in 9 minutes, and was 31·75 mm. Hg. higher than the average systolic pressure observed before the experiment began. The diastolic pressure remained unaffected, but the pulse was slowed about 5 minutes after the drug had been administered, and remained somewhat slow for about 25 minutes. No

palpitation was noticed on this occasion.

Table XIV. shows the effect of ·06 gram. of tyramine on the blood-pressure and pulse-rate of G. H., a healthy male subject, aged 32.

This subject's systolic pressure was elevated 4-7 minutes after the drug had been administered, and remained high for

TABLE XII.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute
7.30	127	62	74
7.50	129	58	76
8.10	127	60	74
8.30	129	61	72
8.35	Tyramine ·08 gram.		
8.37	136	65	72
8.40	162	60	64
8.45	164	60	64
8.50	166	60	64
8.55	160	60	64
9	152	62	68
9.5	150	60	72
9.10	144	62	72
9.15	136	62	70
9.20	130	64	72
9.25	130	65	70
9.30	132	68	68
9.35	134	67	70
9.40	135	66	68
9.45	130	63	74
9.50	129	66	74

25–30 minutes. The maximum height (182 mm. Hg.) was attained in 17 minutes, and was 41 mm. Hg. higher than his average systolic pressure observed before the experiment began. The diastolic pressure was unaffected. The pulse-rate was slightly slowed 8–12 minutes after the drug had been administered, and remained rather slow for 10–15 minutes. Slight palpitation was complained of about 10 minutes after the

drug had been administered, and lasted for about 5 minutes.

The effect of tyramine in all my experiments was to cause a considerable elevation of the systolic pressure; this effect was apparent in from two to seven minutes, and lasted for from ten to fifty minutes. It did not appreciably affect the diastolic pressure, and, except for slight transitory palpitation on two occasions, it caused no unpleasant symptoms. It seems to be an effective and safe blood-pressure elevator, and I think that,

TABLE XIII.

Time. p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.
5.75	123	70	70
5.50	120	66	70
[illegible]	122	65	68
6.38	120	65	68
6.41	Tyramine ·08 gram.		
6.43	127	68	68
6.49	147	60	64
6.50	153	65	60
6.55	149	58	60
7	142	65	60
7.5	146	68	60
7.10	138	69	64
7.15	136	71	68
7.20	131	69	66
7.30	126	68	70
7.40	122	66	68

injected hypodermically or intravenously, it should prove of great value in emergencies.

* * * * *

Series of observations, continued in each case for over an hour after the administration of the drug, were made on the effect of atropine, camphor, cotarnine, digitoxin, ergotoxin, and strychnine on the blood-pressure of the test subject. Only short notes of those observations are given, as the results were in every case negative. My observations on the effect of those

drugs have led me to the conclusion, that they are of no value as blood-pressure elevators, when administered to the human subject in medicinal doses.

TABLE XIV.

Time, p.m.	Systolic Pressure in mm. Hg.	Diastolic Pressure in mm. Hg.	Pulse Rate per Minute.
5.50	140	75	76
6.10	142	80	72
6.30	142	78	72
6.50	140	75	74
6.53	Tyramine ·06 gram		
6.56	141	80	72
7	154	81	72
7.5	175	77	66
7.10	182	75	68
7.15	166	80	66
7.20	162	75	72
7.25	148	78	70
7.30	144	76	68
7.35	140	74	72
7.40	142	74	72

ATROPINE.

Three series of observations were made on the effect of atropine sulphate, one series on the effect of $\frac{1}{100}$th grain and two series on the effect of $\frac{1}{50}$th grain. In no case was the systolic or diastolic pressure appreciably affected. The pulse-rate appeared to be somewhat slowed by $\frac{1}{100}$th grain of atropine sulphate, and accelerated by $\frac{1}{50}$th grain. Some dryness of the mouth was noticed on each occasion.

CAMPHOR.

The effect of camphor was investigated on four occasions. The preparation used was a sterilized solution in olive oil. The effect of ·1 gram. (1·5 grains) was investigated on one occasion, the effect of ·2 gram. (3 grains) on two occasions, and the effect of ·3 gram. (4·5 grains) on one occasion. In no case was the drug observed to have any effect on the blood-

pressure or pulse-rate.

COTARNINE.

Three series of observations were made on the effect of cotarnine hydrochloride; two series were made on the effect of $\frac{1}{2}$ grain, and one series was made on the effect of 1 grain. In no case was any appreciable effect on the blood-pressure or pulse-rate observed, nor were any unusual sensations experienced.

DIGITOXIN.

Digitoxin is said to be much the most active principle of digitalis, and to act more powerfully on the vessels than some of the others. Five series of observations were made on the effect of this drug. Three different preparations, two said to contain a large proportion of the glucoside and one a considerable amount of it, were used. One series of observations was made on the effect of $\frac{1}{250}$th grain of digitalin (crystalline), two series were made on the effect of $\frac{1}{60}$th grain of digitalin (amorphous), and two series on the effect of 15 min. of digalen, a sterile standardized solution of amorphous digitoxin (Cloetta). In no case was any effect on the blood-pressure or pulse-rate observed. In every case, a rather severe local reaction about the site of injection occurred, which was least marked in the case of digalen.

ERGOTOXIN.

The effect of ergotoxin was investigated on four occasions. The preparation used was a soluble salt manufactured by Burroughs Wellcome & Co. The nature of this salt I am not at liberty to divulge, but the makers assured me that it was not likely to decompose into ergotinine. Two series of observations were made on the effect of $\frac{1}{100}$th grain, and two series on the effect of $\frac{1}{50}$th grain. In no case was any appreciable effect detected.

STRYCHNINE.

Three series of observations were made on the effect of this drug on the test subject, the hydrochloride of strychnine being used. The effect of $\frac{1}{15}$th grain was investigated on one occasion, and the effect of $\frac{1}{10}$th grain on two occasions. In no case was the blood-pressure appreciably affected; the pulse-

rate was slightly accelerated on one occasion after the administration of $\frac{1}{10}$th grain, but was unaffected by the other doses investigated.

CONCLUSIONS.

1. *Atropine, camphor, cotarnine, digitoxin, ergotoxin,* and *strychnine* appear to be of no value as blood-pressure elevators.

2. *Adrenalin* appears to be a dangerous drug, which should always be used with caution and never as a general blood-pressure elevator.

3. *Eserin* is an effective blood-pressure elevator, but, on account of the distressing nausea, vomiting, and faintness it produces, its use in cases of hypotension does not seem advisable.

4. *Pituitary extract* was found to have no pressor effect in my experiments. I have suggested that its effect in cases of marked hypotension may be different, but I consider it of doubtful value.

5. *Tyramine* appears to be a safe and effective blood-pressure elevator.

THE ADMINISTRATION OF THE "NAUHEIM" TREATMENT IN ENGLAND.

By LESLIE THORNE THORNE, M.D., B.S., etc.

Late Medical Examiner L.C.C. Technical Education Board.

The fact, that the Nauheim treatment for diseases of the heart and circulation can be given in England with results as successful as those obtained at Nauheim, cannot be known too widely amongst the medical profession at the present time, for there is little doubt that it will not be possible to send patients to German or Austrian spas for some years to come. Under these circumstances, it is satisfactory to know that, as far as the balneological treatment of diseases of the heart and circulation is concerned, the administration of the treatment at home has proved in every way as efficacious, and the results obtained have been as good, as those following a visit to Nauheim.

For the last nineteen years, I have practised the administration of this treatment in London, and during this time I have treated a very large number of cases. This has afforded me many opportunities of comparing the results of a course of baths taken at Nauheim with those of a previous or subsequent course in London. It seems to me, therefore, that this is an opportune moment to give a short account of my observations, together with the histories of a few cases typically suitable for treatment by these methods.

There is no doubt whatever that the effects produced upon the heart and vessels by artificial Nauheim baths are identical with those obtained at the natural springs. I have carried out experiments both at Nauheim and in London, taking records before, during, and after various forms and strengths of baths, and the results have been practically identical in all cases.

The effect produced by immersion in a Nauheim bath upon a patient suffering from cardiac dilatation, raised blood-pressure, and the accompanying more or less degenerate and flabby

cardiac muscular tissues, is threefold:—

(*a*) *All the cutaneous capillaries dilate.*—A fall in the blood-pressure is caused thereby, with consequent lessening of the resistance to be overcome by the cardiac contraction.

(*b*) *The cardiac action is strengthened and its frequency diminished.*—This is a natural result of diminished cardiac strain, and can be illustrated by watching the pulse, which exhibits a larger volume and a slower rate, or by polygraphic tracings, taken before and after a bath.

(*c*) *The cardiac conductivity is stimulated.*—In cases in which auricular or ventricular premature contractions are present, showing the existence of an impaired conductivity, such premature contractions often disappear or markedly decrease in frequency during a bath.

From the above, it will be seen that the results we obtain from a course of Nauheim baths are: a slower and stronger cardiac contraction, an improved cardiac conductivity, and a lessened resistance for the heart to overcome. These results are aimed at in all forms of treatment used for cases, exhibiting symptoms of overworked and failing cardiac contraction.

CASES SUITABLE FOR TREATMENT.

The selection of cases suitable for treatment is one of degree rather than of kind, and it is quite erroneous to suppose that the presence of valvular disease contraindicates treatment by the Nauheim methods. As will be seen from the examples given below, very great benefit may be obtained in patients suffering from valvular disease; not that the valvular defects themselves can be cured, but the cardiac dilatation, resulting from the overwork of a defective organ, can be greatly reduced, and in many cases cured for a long period. It is clearly obvious, given a case of mitral regurgitation, that regurgitation is increased, if the heart is dilated as well, and is reduced to a minimum, when the cardiac muscle is toned up and the dilatation reduced. Hence, many of the painful and dangerous symptoms, which are manifested in a

case of dilated, overworked heart with a defective valve, are greatly alleviated or entirely disappear during a course of Nauheim baths. My excuse for laying stress upon the above is, that I have often been told by medical men that they had been led to believe that the Nauheim treatment was of no good when valvular defect was present. I can only say that those responsible for this belief have had either a very unfortunate, or a very limited, experience of the treatment (Cases I. and III.).

Nearly all cases of dilated hearts with enfeebled, and sometimes degenerate, cardiac muscle tissue respond more quickly to this treatment than to any other, and it is particularly suitable for those in which a lengthy course of rest and cardiac tonics has failed to cure dilatation or relieve symptoms. The influenzal heart may be instanced as typical of this class of case.

The dilated, overworked heart, the result of a gouty constitution and an accompanying high arterial tension, derives great benefit from this treatment; the cardiac dilatation is relieved, the blood-pressure gradually drops, and the patient begins to feel the benefit almost from the first (Case IV.).

All cases of cardiac poisoning from diseases, such as enteric or malaria, or from drugs, such as tobacco, are greatly benefited by this treatment, as well as cases of heart-strain due to over-exertion in athletics or work.

The anæmic patient with a dilated heart, who derives no permanent benefit from iron or arsenic, often responds splendidly to a course of Nauheim baths, in conjunction with drug treatment. The irritable, nervous heart of the neurasthenic is often benefited by a course of treatment, but the results in these cases are not so satisfactory as in organic defects, such as dilatation from degenerate heart muscle and high blood-pressure, for the nervous heart is, in my opinion, one of the most unsatisfactory and difficult conditions to treat.

Cardiac conditions in which symptoms of a defective conductivity, such as constant auricular or ventricular premature contraction, are present, are greatly benefited by this treatment, the cardiac irregularities often disappearing during and after treatment (Cases I. and II.). Good results have been reported

in cases of heart-block of various degrees, but my own opinion is that many cases which have developed heart-block are not suitable for this treatment. Cases of auricular fibrillation are not suitable for the Nauheim treatment, but should be treated with large doses of digitalis to reduce heart-block.

Cases of chronic nephritis, exhibiting signs of cardiac dilatation, will often respond well to the treatment, the dyspnœa, cardiac pain, and orthopnœa disappearing during treatment. In these cases, the baths must be given warmer than usual, and no carbonated baths must be used. It is a common mistake to believe that a Nauheim bath is always a carbonated bath; this is quite *erroneous*, and is a fertile cause of failure and disappointment in treatment. No heart case is ever treated at Nauheim with *carbonated* baths at the commencement of the course, and a large percentage of the cases have the entire course of *still* baths. Many cardiac cases are only harmed by *carbonated* baths, but are greatly benefited by a course of *still* baths. No one should attempt to give Nauheim baths without carefully reading up the subject beforehand, and the custom of leaving the details, *i.e.*, length, strength, and temperature, to a nurse who professes to understand their preparation, cannot be deprecated too strongly.

It is not possible in a short article to give in detail a description of all cases which derive benefit from the Nauheim treatment, but the following examples are illustrative of its wide range of usefulness.

Case I.—The patient, a man aged 57 years, was sent to me by Dr. W. H. Gregory of Beverley, who informed me that he was suffering from mitral regurgitation, cardiac dilatation, and muscle failure. He had been confined to his bed for eight weeks on account of palpitation, dyspnœa, insomnia, general weakness, and very intermittent pulse, and had improved to a certain extent, but for some time had been at a standstill. The patient had had rheumatic fever, accompanied by pericarditis and endocarditis, when he was 14 years of age. When I first saw him, he was very thin and weak, and could not walk many steps without having to sit down; he was distinctly cyanosed, and dyspnœa was present on slight exertion. His pulse was very small, and exhibited premature auricular contractions (Fig. 1); and he was unable to sleep without a narcotic, and suffered much from dyspepsia.

The area of absolute cardiac dullness extended from two inches to the right of the right border of the sternum to the left nipple line, the apex beat being just inside the left nipple line; a loud blowing systolic

murmur was heard all over the cardiac area, but was most intense at the apex, and was conveyed into the axilla. His blood-pressure was 75–125 mm. Hg. The case was undoubtedly one of cardiac dilatation, due to weakening of the myocardium and mitral regurgitation. He gradually improved under treatment, and before the end of the course of 25 baths, extending over five weeks, he had lost the dyspnœa, palpitation, and dyspepsia, could walk

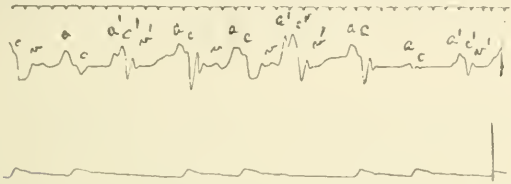

Fig. 1.—*Polygraphic tracing of Case I. before treatment, showing a pulse of small volume exhibiting frequent premature auricular contractions (a c' v'), two examples of which are shown, the a-c interval is normal. The premature contractions are not strong enough to produce any effect upon the radial pulse.*

for a quarter of an hour to 20 minutes, and slept fairly well with a very occasional narcotic. His cardiac dullness had decreased to normal, extending from the left border of the sternum to two inches inside the left nipple, the systolic murmur was very much softer and much less diffuse. He returned home to Yorkshire, and was able to walk about his grounds with comfort, and to go up and down stairs, which he had not been able to do since the beginning of his illness.

I saw this patient five months after treatment, when he informed me that he could keep about all day, slept and ate well, and had no dyspepsia. His cardiac dullness was still absolutely normal, and the pulse was quite regular and of good volume (Fig. 2).

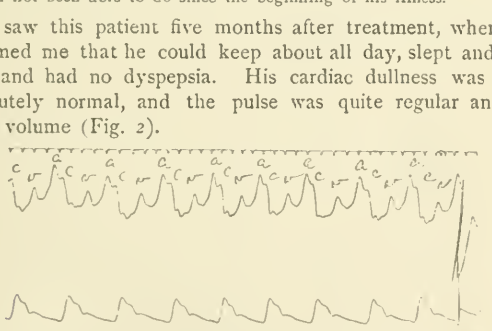

Fig. 2.—*Polygraphic tracing of Case I. five months after treatment, showing a perfectly regular pulse of much improved volume. The a-c interval is normal, pulse-rate 68 per minute.*

I saw the patient again seven months after treatment, he was still keeping quite well, the cardiac dullness was normal,

and the pulse was regular and of good volume (Fig. 3).

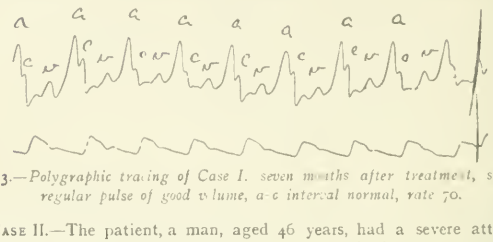

Fig. 3.—*Polygraphic tracing of Case I. seven months after treatment, showing regular pulse of good volume, a-c interval normal, rate 70.*

Case II.—The patient, a man, aged 46 years, had a severe attack of multiple abscesses, which was followed by a spell of very arduous work during the winter and spring. In the early summer, he began to suffer from general ill-health accompanied by constant cardiac irregularity, which caused great discomfort and insomnia. Treatment with bromides and digitalis relieved him for a time, but as he found the relief only temporary, and was not able to do his work without great fatigue, he consulted me. I found him to be suffering from a very dilated and weakened heart, exhibiting constant irregularities. The absolute cardiac dullness extended from an inch outside the right border of the sternum to the left nipple line, measuring at the level of the nipple six inches. The heart sounds were slapping at the apex, and scarcely audible at the base. The polygraphic tracing exhibited premature contractions of varying kinds, some auricular and some ventricular, but of so feeble a character that they did not reach the radial pulse (Fig. 4).

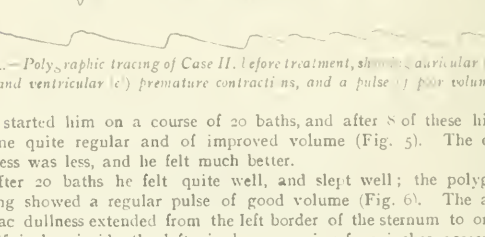

Fig. 4.—*Polygraphic tracing of Case II. before treatment, showing auricular (a c v) and ventricular (c) premature contractions, and a pulse of poor volume.*

I started him on a course of 20 baths, and after 8 of these his pulse became quite regular and of improved volume (Fig. 5). The cardiac dullness was less, and he felt much better.

After 20 baths he felt quite well, and slept well; the polygraphic tracing showed a regular pulse of good volume (Fig. 6). The area of cardiac dullness extended from the left border of the sternum to one and a half inches inside the left nipple, measuring four inches across. The sounds at the apex were natural, and those at the base could be well

heard.

The patient went away intending to take a month's holiday. He indulged in a good deal of golf, and returned to London and work in

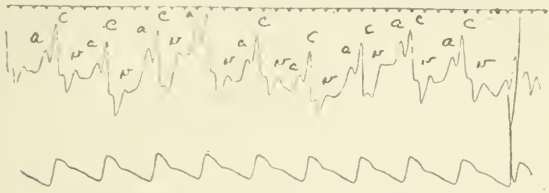

Fig. 5.—*Polygraphic tracing of Case II. after 8 baths, showing a regular pulse of improved volume. Rate, 75 per minute.*

10 days, but he was not really fit for work, and consequently had a relapse. After about 10 days' work, he was forced to take a month's rest, since when he has been perfectly well, and able to work hard and play golf.

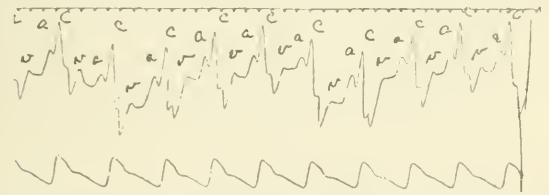

Fig. 6.—*Polygraphic tracing of Case II. after 18 baths, showing regular pulse of good volume.*

Case III.—The patient, a man aged 41 years, was brought to me by Dr. Johns of Bournemouth. The history of the case is as follows:—Two years previously, he was suddenly seized with violent pains in the left side of the chest and left arm, accompanied by severe shortness of breath. These attacks increased in severity and frequency, despite various forms of treatment, and for over a year he had been an absolute invalid, unable to do anything for fear of bringing on an attack. He could scarcely eat anything, had very broken nights on account of the frequent recurrence of these attacks, and had lost a good deal of weight. The only treatment that alleviated the attacks was the use of amyl nitrite capsules, of which he was using 40 to 50 in the 24 hours, his attacks of pain coming on about every half hour. No definite cause could be discovered for his condition, except that he had been a fairly heavy drinker for years.

When Dr. Johns first brought him to see me, he looked very ill, was very anæmic and cyanosed, and suffered from dyspnœa, even whilst sitting still. He was very thin, and though a tall man, only weighed 9 stone 7 lbs. His pulse was 100 per minute, a typical pulse of aortic regurgitation, violent pulsation could be seen in the neck and in all vessels near

the surface, and his whole arm pulsated with each heart-beat; his blood pressure was 40–190 mm. Hg.

On examination of the chest, the impulse was seen to be general over the whole of the left front, and at the apex, 2 inches outside the left nipple line, it was very forcible and diffuse; the area of absolute cardiac dullness was exceedingly large, extending for 2½ inches to the right of the sternum to 2 inches to the left of the left nipple, and measuring 8 inches across on the nipple level. On auscultation, a loud double murmur could be heard over the aortic area, and a strong blowing systolic over the apex, conveyed into the axilla. He had two attacks of angina whilst in my consulting room. On each occasion he became very white, the dyspnœa was greatly increased, and the symptoms were not relieved till he had used a capsule of nitrite of amyl. He was undoubtedly suffering from a greatly dilated and hypertrophied heart, accompanied by double aortic disease, mitral regurgitation, and frequent attacks of angina pectoris. A polygraphic tracing of his pulse showed a rapid pulse, 93 per minute, and a decidedly increased a–c interval, indicating impaired cardiac conductivity (Fig. 7). The rounded apex to the radial pulse tracing was caused by the necessity of pressing the pen heavily upon the paper, in order to prevent the whole breadth being taken up by the violent movement of the radial curve.

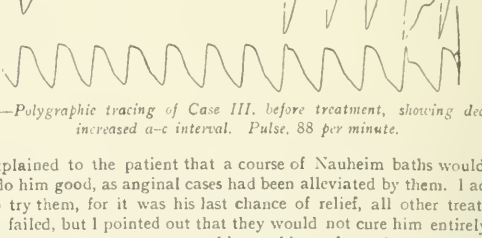

Fig. 7.—*Polygraphic tracing of Case III. before treatment, showing decidedly increased a–c interval. Pulse, 88 per minute.*

I explained to the patient that a course of Nauheim baths would most likely do him good, as anginal cases had been alleviated by them. I advised him to try them, for it was his last chance of relief, all other treatments having failed, but I pointed out that they would not cure him entirely, and that the good, so severe a case as his would get from the treatment, was uncertain. He decided, however, to try a course, for he said, that if he went on very long as he was, the pain and the insomnia would kill him. He started a course of baths, at which time he was using from 40 to 60 capsules of amyl nitrite in the 24 hours. He began to improve from the first, the attacks of angina decreasing in number and severity; after 10 days' treatment, during which time he had had 8 baths, he was only using 16–20 capsules in the 24 hours. After 19 baths, extending over a period of 25 days, he was sleeping and eating well, had put on 1 stone 3 pounds in weight, his weight being 10 stone 10 pounds, and he seldom used a capsule of amyl nitrite during the day, but still used from 6 to 8 during the night. His pulse was slower, 78 per minute, and the a–c

interval was normal (Fig. 8).

The cardiac dullness was decidedly less, measuring 6 inches across at the level of the nipple, and extended from 1 inch to the right of the sternum to 1 inch to the left of the left nipple; the apex beat had come in as well, and was 1 inch outside the nipple line. Both the pulsation and the murmurs were much reduced in strength, and the maximum blood pressure was only 145 mm. Hg.

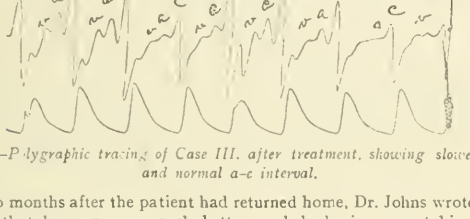

Fig. 8.—*Polygraphic tracing of Case III. after treatment, showing slower pulse and normal a–c interval.*

Two months after the patient had returned home, Dr. Johns wrote to me to say that he was very much better, and had given up taking amyl nitrite, as he never had an attack of angina, two months later he again wrote, as follows:—"Still more wonderful reports of our patient B.—He has now put on two stone in weight, sleeps well, eats well, has no pain, and the murmurs have changed in character, being much softer." This patient was so seriously ill, when I first saw him that I hardly expected the treatment to have so highly satisfactory a result.

Case IV.—The patient, a man aged 63 years, was of a gouty constitution, and had been used to a good quantity of alcohol. He had a bad attack of influenza 15 months before I saw him, and had been failing in health ever since. For nine months, he had suffered from severe asthma and bronchitis, and had been kept to bed and a bath-chair; he had, in fact, been told to buy a bath-chair and a carrying chair, for there was little chance of his being well enough to walk again. When I first saw the patient, he looked ill, and was very cyanosed and short of breath; said he could neither eat nor sleep, having to be propped up at night, and suffered greatly from depression. He was puffy under the eyes, the pulse was 108 per minute, and exhibited constant irregularities, the result of premature ventricular

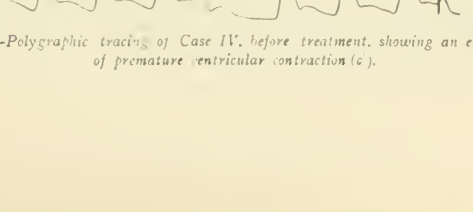

Fig. 9.—*Polygraphic tracing of Case IV. before treatment, showing an example of premature ventricular contraction (c').*

contractions. The heart was very dilated, the area of absolute cardiac dullness measuring six and a half inches across at the nipple level and extending two inches to the right of the sternum, the apex beat was just in the left nipple line, and the heart sounds were very feeble. The arteries were thickened and tortuous, the blood pressure was 80 150 mm. Hg., and his liver dullness extended from two inches above the normal to an inch below the costal arch. I gave this patient a course of 25 Nauheim baths extending over a period of five weeks. After three weeks' treatment, he was so much improved that he could walk from a mile to a mile and a half, and therefore sold his bath-chair and carrying chair. At the end of the treatment, he slept and ate well, had no dyspnœa or orthopnœa, and could walk two or three miles with comfort. His heart sounds were much stronger, his cardiac dullness was normal, extending from one inch and a half inside the left nipple to the left border of the sternum; the apex beat was one inch inside the left nipple line, and the liver dullness had decreased by two inches. The pulse was of better volume and perfectly regular in time, 60 per minute (Fig. 10), and the blood pressure had fallen to 70-125 mm. Hg.

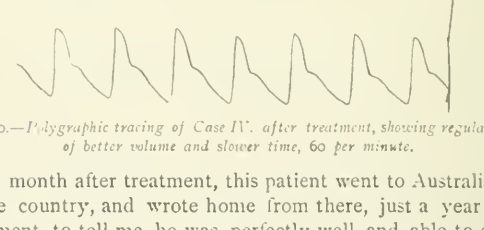

Fig. 10.—*Polygraphic tracing of Case IV. after treatment, showing regular pulse of better volume and slower time, 60 per minute.*

A month after treatment, this patient went to Australia, his native country, and wrote home from there, just a year after treatment, to tell me he was perfectly well, and able to enjoy long walks.

CONCLUSIONS.

1. The "Nauheim" treatment can be given in England, with results quite as satisfactory as those obtained at Nauheim.

2. In many cases, when treatment by rest and heart tonics has failed to give relief, it has proved successful.

3. In cases of valvular defects, with weakened and dilated myocardium, it is quite as successful in reducing dilatation and relieving symptoms as in uncomplicated cases of myocardial weakness.

4. The use of carbonated baths *in the early stages* of the treatment is, in most cases, harmful.

RECENT WORK ON DISEASES OF THE HEART.

By CHARLES W. CHAPMAN, M.D., M.R.C.P., etc.

Senior Physician to the Hospital for Diseases of the Heart, Soho Square, etc.

MYOCARDITIS.

Alexander Lambert (*New York Journal of Medicine*, November, 1913) contributes a paper on *Pain and other Clinical Manifestations of Myocarditis* in which, while acknowledging the great value of modern methods in the diagnosis of this affection, he writes we must still fall back on the clinical observations of the different forms of myocardial degenerations, and estimate from them the form of myocarditis present. The differential diagnosis is thus given; the slappy valvular sound with much diminished muscle note in dilatation; the silent one with weak muscular tone in the fibroid variety; the sound full and of lower tone than usual in fatty degeneration; the sounds of the fœtal type in brown atrophy; the galloping rhythm is significant of muscular degeneration, it is found in chronic nephritis, infectious diseases, and in diphtheria, when it is of bad import. Early dyspnœa on exertion with pain in the side are early signs. The author calls attention to Head's observations that the distribution of pain and hyperæsthesia bears a close relation to the chambers of the heart most affected; thus in the auricles it is the lower axilla and the shoulder blades, while in the ventricles they are referred to the chest wall, inner aspect of the upper arm and ulnar surfaces of forearm and wrist. The severest pain is associated with coronary and aortic lesions. Pain in the cardiac region is suggestive of cardiac change, but when unaccompanied by breathlessness and negative stethoscopic examination the prognosis is good.

THE HEART IN SYPHILIS.

Ruggles (*New York State Journal of Medicine*, November, 1913) remarks, *inter alia*, on the importance of recognizing syphilis as a factor in heart disease. He states that nearly all

aortic aneurysms and 85 per cent. of all aortic valvular lesions are syphilitic in origin, and can be influenced favourably by salvarsan in most instances, while many may be cured by the same treatment. Angina pectoris and heart failure, in otherwise healthy persons with no history of rheumatism, should lead to a suspicion of syphilis. The present writer can endorse these statements in the main, but it is too early to speak of cures by salvarsan.

That syphilis is not always the cause of aortic aneurysms is shown by the following case. It is, however, to be noted that the Wassermann test does not seem to have been applied. Dr. J. A. Glover, at the clinical section of the R.S. Med. (May, 1914), related a case of rupture of an abdominal aneurysm in a lady aged 34. There was no history of rheumatic fever, severe strain, or syphilis, and the patient had had good health. The first symptom was a sharp pain in the back while ascending a slight hill, which the patient attributed to lumbago. Eleven hours later, she was found blanched, unconscious, pulseless, and apparently dying. As a large mass was found in the right groin, appendicitis was suspected, but at the operation the appendix was found to be healthy. The patient died 24 hours after the operation. At the post-mortem, a ruptured aneurysm about the origin of the renal artery was found. That a serious lesion of the abdominal aorta was not suspected is not surprising when, as the speaker remarked, aneurysms of the abdominal aorta amount to scarcely 5 per cent. of the total of aneurysms. Of these only $\frac{1}{10}$ occur in females.

An editorial (*New York Medical Journal*, November, 1913) refers to the demonstration in the secondary stage of spirochetes in the cardiac muscle by Buschke and Fisher in 1906, and to Harlow Brooks (*American Journal of Medical Science*, October, 1913), who states that syphilis has a special affinity for the coronary arteries. He believes, that the apparent rarity of cardiac involvement is due to the relative infrequency with which true gumma of the heart is found post-mortem. Dr. Brooks found in his series of autopsies, that death occurred in 66 per cent. of his syphilitic cases as a result of, or in association with, serious circulatory disease, apparently of syphilitic origin. The myocardium was found seriously diseased

in 44 out of 50 cases, but cardiac gumma only in 5. One patient died before the secondary rash had fully appeared, owing to a minute perforation of the aorta. An acute arteritis and periarteritis was found throughout the myocardium and the vasa vasorum of the aorta. In early and late cases, irregularity of the heart's action is the most frequent clinical manifestation; the history, general aspect, and the Wasserman reaction indicate the true ætiology. Several successful results have followed the exhibition of salvarsan, but alarming symptoms supervened where the pulse was slow and irregular.

H. Brooks (*American Journ. Med. Sci.*, October, 1913) believes that lueitic involvement of the heart and aorta is much more frequent and much more serious in its direct effects than has been generally conceded by internists or even by syphilographers. As there are no definite pathognomonic signs, recourse to the Wasserman test is recommended. Preventive treatment during the active period of the secondary stage is recommended.

CANE-SUGAR IN THE TREATMENT OF CHRONIC HEART DISEASE.

Dr. Goulston's contributions on this subject have been noticed in a previous review. The conclusions arrived at by the author may be summed up as follows:—The central difficulty in all chronic cases of heart disease is due to malnutrition of the musculature of the heart, that this is largely caused by a deficiency of glycogen, which can be supplied by the ingestion of dextrose in the form of cane-sugar only. The author quotes the opinion of physiologists that "both in the sino-auricular node and in the auriculo-ventricular bundle and its connections there is a remarkable amount of glycogen." The craving for chocolate and jam by our soldiers in the present campaign tends to confirm this. Since the use of cane-sugar in heart disease is avowedly recommended as an aid to other measures, there is no reason why the treatment should not have an extended trial.

ANGINA PECTORIS.

Graham Steele (*Med. Chronicle*, November, 1913) refers to the combination of pericardial friction sounds with other signs of angina pectoris. Dealing first with pericarditis, the writer recognizes that friction sound may be absent in the presence of

conditions which usually occasion it, and that friction may be present without inflammatory exudation on the pericardial surfaces. Cases bearing on these points are given. The similarity in the areas of dulness in pericardial effusion and cardiac dilatation is pointed out; the extension upwards in the latter is due to the distended infundibulum of the right auricle, that to the right to the right auricle, and to the left to the left ventricle. The writer considers that the friction sounds he has noted in cases of angina pectoris are not due to pericarditis, but to "a nutritive disturbance in the pericardial surfaces, sufficient to interfere with their normal noiseless gliding upon each other."

THE USE OF DIGITALIS IN PRACTICE.

R. D. Rudolph (*Canada Lancet*, March, 1914), in reminding us of Withering's directions for the use of digitalis, written in 1785, shows how correct his conclusions were based, as they must have been, solely on clinical observation. Withering gives an old Shropshire woman credit for a recipe, in which he recognized digitalis as the essential drug among twenty other ingredients. Withering wrote: "Let the medicine (Gr. 1–3 of the powdered leaf) be taken twice a day and continued until it acts either on the stomach, kidneys, pulse or bowels; let it be stopped on the appearance of any of these effects, and I will maintain that the patient will not suffer from its exhibition nor the practitioner be disappointed in any reasonable expectation." By such treatment, not only would dropsy be relieved, but he found the drug "had a power over the motion of the heart to a degree as yet unobserved in any other medicine." These remarks are as true to-day as when they were written, though much has been added to our knowledge of the action of digitalis through modern research aided by instrumental methods. The writer agrees with recent observers in his preference for ordinary digitalis preparations to the numerous special ones on the market, none of which give the full effects of the drug. He points out as well that digitalis has very little effect on the normal heart, and that Cushney has shown that in dogs digitalis does not lessen conductivity, as it undoubtedly does in human hearts in which it causes lengthening of the a–c interval.

The value of the drug is best seen in cases of dropsy with

irregular hearts in a condition of auricular fibrillation, but not in the simply rapid heart of toxemia. While agreeing with the modern teaching that digitalis does not materially increase blood-pressure, he quotes Marovis's experiments last year on healthy students, in which a single dose of ♏ 20 of Tr. Digitalis caused a rise of 13 m.m. of Hg., with an average slowing of eight beats. The author quotes a case of a dropsical man in the hospital with a blood-pressure of 120, in whom digitalis caused a rise of 100 m.m., and who left the hospital with a pressure of 220, yet feeling much better. In this case 220—the patient's normal pressure—was attained on the establishment of compensation.

HYPERTENSION.

J. L. Miller (*Journal, A.M.A.*, October, 1913), in his paper, discusses the clinical aspects of hypertension, especially with regard to the renal factor, which increased knowledge has shown to be more important than the arterial. He thinks it possible that some changes in the adrenal secretion may account for the renal changes. It is possible, he thinks, that if urinary examinations were made with greater frequency, many patients with apparently normal urine would reveal the presence of albumen and casts. Cerebral hæmorrhage, cardiac incompensation (including angina), and uræmia are the most frequent causes of death. It is often difficult to make a prognosis, on account of our ignorance of the strength of the arterial wall and the working power of the heart muscle. Men are less liable to show symptoms of hypertension than women, especially obese women. Transitory cerebral disturbances are ominous, and moderate œdema of the feet is of graver significance than when due to heart disease. The care that a patient can give himself as regards mental or physical over-exertion, chilling, habits, etc., is of extreme importance. Attention to elimination, dietetics, and general hygiene is of more importance than drug treatment. When cardiac incompensation develops, digitalis should be used as in other forms of incompensation. There is no good evidence that iodides are of any special value, except in syphilitic cases. With regard to the last paragraph, the present writer would refer the reader to the section "The heart in

syphilis."

HIGH AND LOW BLOOD-PRESSURE

W. J. Stone (*Journal, A.M.A.*, October, 1913) gives the result of his observations in the study of pulse-pressures in 170 persons, to determine what clinical significance was attached to certain high and low auscultatory readings. The subjects were both normal and physiological, including cases of acute infections, those with arterial hypotension and hypertension, and various compensated and uncompensated heart lesions. His conclusions are—

(1) The determination of systolic and diastolic blood-pressures by the auscultatory method is to be preferred to the palpatory method for systolic and column indicator oscillation for diastolic, because of greater accuracy.

(2) The readings are slightly higher by the auscultatory method than by the palpatory.

(3) The pulse-pressure measures the energy of the heart in systolic in excess of the diastolic pressure. For clinical purposes, it represents the load of the heart. Under normal conditions, it is approximately 50 per cent. of the diastolic pressure. The myocardial load may, therefore, be expressed by the fraction

$$\frac{\text{pulse-pressure}}{\text{diastolic pressure}} \text{ or } \frac{\text{P.P.}}{\text{D.P.}}$$

(4) Since the diastolic pressure measures the peripheral resistance, it is a better index of hypertension than the systolic pressure. A sustained diastolic pressure of 100 to 110 signifies hypertension. The diastolic is less influenced by physiological factors than the systolic pressure alone.

(5) The comparison of systolic and diastolic pulse-pressures is of clinical value in the interpretation of circulatory changes, and of more importance than the estimation of systolic pressure alone.

(6) In arterial hypertension and myocardial decompensation, in a broad sense, the blood-pressure and heart load are increased, as a rule, the overload factor varying greatly, from 30 to 175 per cent. in this series. The greater the overload factor, the greater was the danger of exhaustion.

(7) In circulatory failure, due to shock, to many acute

infections, and hæmorrhage, the blood-pressure is low. This is the result, it is believed, of factors which have influenced arterial tonus, peripheral resistance with rapid pulse rate, increased respirations, and lowered venous pressure.

(8) In acute affections, a sustained pulse-pressure warrants a more favourable prognosis, as a rule, than a low pulse-pressure, other things being equal, although the change from normal to a low pressure in circulatory failure may occur very rapidly. As a rule, the lower the pulse-pressure, the greater the danger of circulatory failure.

(9) From this point of view, low pulse-pressure in circulatory failure involves the consideration of complex peripheral changes, in addition to the myocardial factor.

(10) The pulse-pressure multiplied by the pulse-rate does not give a reliable index of systolic output in circulatory shock, since the pulse-rate clinically increases out of proportion to the fall of pulse-pressure. This shortens the time during which the left ventricle is filled during diastole, and lessens the systolic output, although by the formula, pulse-rate multiplied by pulse-pressure, the unit volume output may appear to be increased.

(11) The pulse-pressure estimations in this series did not show marked variations from day to day in neurotic persons.

DIASTOLIC BLOOD-PRESSURE—CLINICAL ESTIMATION OF.

Lancet, December 5, 1914. In this annotation, attention is drawn to the clinical value of the estimation of diastolic blood-pressure, and of the auditory method of McWilliam and Melvin. The only instrument necessary is a Riva-Rocci sphygmomanometer or a modification of it. The armlet must be applied sufficiently high in the upper arm, to allow of the chest piece of a binaural stethoscope to be placed on the brachial artery. When the systolic blood-pressure has been obtained, the stethoscope is applied. No sound will be heard until the pressure is gently relaxed, when pulsations will be heard. These are (1) sharp, clear sound; (2) muffled or murmurish; (3) loud and clear; (4) dull; (5) abolition of sound. The diastolic pressure is to be noted on the scale when 3 gives way to 4. The test is of no value in aortic disease, for here, even in the absence of any constriction, a murmur may be heard The present

writer can testify to the value of this method and to the superiority of the Riva-Rocci instrument over the ossilometer of Pachon in this particular investigation. For further details see *Heart* (1914, 5, 153) and *Quarterly Journal of Med.* (1914, 5, 419).

AURICULAR FLUTTER.

Hay, J. (*Lancet*, 1913, p. 986), relates two cases, one aged 40, seen in 1906, when the auricles were 270, ventricles 90 (3-1 block); two years later, auricles 240, ventricles 60 (4-1 heart block), patient not so well. Three weeks' treatment with squills brought on fibrillation. After six years, the heart-rhythm was quite normal, and the patient fairly well.

The second case, that of a man, 62 years of age, whose heart had been rapid and irregular for 10 years; polygraphic examination showed auricular flutter. Auricles, 300; ventricles, 50–60, and coupled. During observation, Cheyne-Stokes breathing and pulsus alterans were noted. Digitalin caused a–v heart block, but not fibrillation. Small doses of digitalin kept the ventricle steady and at a moderate rate.

CONDUCTION DEFECTS IN THE HEART.

Matthewson, G. D. (*Edin. Med. Journ.*, 1913, 11, 233), states that defects in conduction may exist in the a–v bundle, or in one or the other of the right and left branches within the ventricular musculature. The string galvanometer will show the form of ventricular contraction, and whether both ventricles contract together as in the normal, or whether one precedes the other, as occurs in defective branch conduction. The writer gives illustrative cases.

THE HEART IN EARLY LIFE.

G. A. Sutherland in this book, focusses the recent work in cardiology in its special application to heart-affections in the young. The importance of a full recognition of functional diseases of the heart, especially that of irregularity, is well brought out. Among the many practical points in the book, a few may be given. On compound irregularities (page 39): "While in cases of organic heart disease a mixed form of irregularity is not uncommon, in the functional disturbances

one definite type is usually present . . If the observer will make the patient hold his breath that form (respiratory) of irregularity will disappear"; and in page 117 we note: "The functional signs are liable to great variation from day to day, with change of posture, and with the general health. The organic signs are more persistent under the above conditions." Page 91, on Paroxysmal Tachycardia we read: "The presence of pulsus alterans is of value in diagnosis, because when associated with tachycardia it may be taken as indicative of a disordered rhythm of the heart." Page 109: "The characteristic presystolic murmur is not developed as a rule until later childhood or youth." And on page 151: "A typical presystolic murmur never develops during an attack of rheumatic fever." Page 124: "Auricular fibrillation is a special form of increased excitability of the auricular walls which leads to marked irregularity of the pulse. The importance of the subject is fully recognized in adult life, but in early life examples of the condition are but rarely met with."

OBLITERATIONS OF THE SUPERIOR VENA CAVA.

Hébrard (*Gazette des Hôpitaux*, August 2, 1913) remarks on the improvement of the prognosis in these cases, since chronic inflammatory conditions of the mediastinum have been shown to bear an important part in bringing about obstruction. The writer enumerates as causes—malignant masses in the vein, thrombosis as a result of such masses, pressure from tuberculous glands, aortic aneurysm, malignant disease, and a chronic mediastinitis. The latter may be due to syphilis, tuberculosis, mediastinal pleurisy, mediastino-pericarditic inflammation, and repeated infections of the respiratory tract. The writer emphasizes the importance of recognizing the frequency of syphilis as a factor. The present writer reported a striking case of obstruction of the superior vena cava by gummatous mediastinitis in Clinical Society's Trans., Vol. 33. Renault is quoted as stating that the superior vena cava is one of the sites of election in tertiary syphilis. Secondary enlarged glands as well may compress the vessel. The results of compression on the superior vena cava are: œdema of the upper part of the body, face, arms, chest, and upper part of abdomen to umbilicus; cyanosis of face; and dilated veins over upper part of the

body.

ARTERIO-SCLEROSIS AND CERTAIN OCULAR CONDITIONS.

Elsworth Smith, of St. Louis (*Interstate Med. Journ.*, May, 1914), in an interesting paper on this subject, shows that much can be done in the treatment of ocular affections, connected with arterio-sclerosis, by recognizing the dependence of the former upon the latter, and the adoption of treatment based on such knowledge. After discussing the general causes of arterial degeneration, special reference is made to hæmorrhagic glaucoma and albuminuric retinitis. The writer proceeds: "We know . . . . for treatment reliance is placed on hyd. perchlor. and pot. iodid., complete rest in bed in serious cases and a life devoid of strain and worry with the avoidance of alcohol and tobacco, extreme moderation in diet, especially as regards meat, purgation when necessary, and the use of vaso-dilators in emergencies."

EXTENSIVE THROMBOSIS IN HEART DISEASE.

F. Glaser (*Med. Klin*, October 19, 1913) records a case of thrombosis following heart disease in which the lower arms, head and neck were involved. The patient, a servant girl aged 24, had rheumatism seven years previously. The cardiac dulness was considerably increased, and the apex-beat was in the anterior axillary line. There was aortic incompetence and both pre-systolic and systolic mitral murmurs. The patient was very anæmic. After three months there was a painful swelling under the right sterno mastoid muscle. There were signs of pulmonary infarct. Nine days later the right side of the face was swollen and the parotids hard and tender. The right arm increased in circumference. After further pulmonary infarcts the patient died. Post-mortem showed incompetence of the aortic and tricuspid valves, stenosis and incompetence of the mitral, endocarditis, hydropericardium, hydrothorax, ascites, jaundice, and thrombosis of the superior vena cava, and of subclavian, and both jugular veins. Such extensive thrombosis the author states to be very rare. He considers chlorosis a probable factor from faulty nutrition of the blood vessels.

THE HEART AND UTERINE FIBROIDS.

McGlin (*Trans. Amn. Gynecol. Socy.*, Vol. 38, 1913), out

of 5,700 autopsies, 244 subjects had fibroid tumours of the uterus. The author states that uterine myomata in middle and advanced life are practically associated with sclerotic heart lesions, part of a general process bearing no relation to the fibroid. Large tumours, by increasing the work of the heart and fibroids, causing pressure on the pelvic circulation, may produce hypertrophy and secondary dilatation of the heart. Anæmias from hæmorrhages, infections and certain degenerations affect the heart secondarily, but these changes in the majority of instances are caused by conditions entirely foreign to the tumour.

Two instructive cases were shown at the children's section, *Roy. Soc. Med.*, on December 11, 1914.

(1) F. J. Poynton showed a boy aged 5 years with (?) aortic disease, whose history was negative except for that of tonsillitis. There was no history of rheumatism in the child or parents, nor of fever. The tonsils were very large and almost meeting. The heart showed no apparent enlargement and the impulse was not forcible. Apex: First sound short and a systolic murmur. Aortic cartilage: rasping systolic murmur conducted upwards and outwards. The chief interest in the case lay in the history of tonsillitis only. The present writer has seen several cases with a similar history. (The Review, THE PRACTITIONER, May, 1914, p. 113.)

(2) E. B. Gunson showed a specimen from a girl aged 15 admitted to hospital suffering from scarlet fever on the thirtieth day of the disease. She had never had rheumatic fever, but had had "growing pains": pericarditis developed on the fortieth day. Death followed four days later. Post-mortem showed severe and extensive pericarditis.

REVERSED ACTION OF THE HEART.

Horatio Williams and H. James ("*Heart*," Vol. 5, p. 109) report a case in which the ventricles contracted before the auricles. The patient, a man 51 years of age, with a Stokes-Adams syndrome. Examination showed that the ventricles were beating 40 to the minute. The initiation of the heart beat by the ventricles was probably due to depression of the sinal rhythmicity below that of the ventricles' intrinsic rhythm. The auricle, therefore, following its customary function, responds to that focus of stimulation which is of the highest

rhythmicity, and which in this case was not the sinus, but the stimulus conducted *up* the bundle of His. The conclusion was rendered possible by means of electro-cardiographic tracings.

HEART DISEASE AND LIFE ASSURANCE.

Hingston Fox, in an article on "Progress of Life Assurance" (*Lancet*, January 17, 1914), remarks, with regard to heart disease, that our first attention is given to the integrity of the heart in its muscular and nervous mechanism. Is it functionally efficient, or is there degeneration or myocarditis? The writer avers that doubtless not a few lives, having a fair prospect of longevity, used to be rejected for assurance on account of valvular defects which were well compensated, and that we are now able to recommend many such cases at an extra rating. The present writer would observe that these remarks apply with increased force to cases for which the period of assurance is limited to a certain number of years.

Under the section "Blood Pressure," in the same paper, it is stated that the data are not large, and the time too short to provide a base for conclusions. In estimating the value of blood-pressure observations, account should be taken of the effects of mental and emotional strain, of active exercise, of posture, and of meals in producing a passing alteration of tension. The immediate and remote effects of tobacco and alcohol should be borne in mind. When these have been excluded, we have to consider transient spasm of the arterial wall or one of more progressive or permanent change a product of alimentary toxæmia or of kidney failure.

SUTURE OF WOUNDS IN THE AURICLE.

Chifolian and Marchak (*Progrès Méd.*, February 7, 1914) report a second case in France in which a wounded auricle had been sutured. 24 cases have been recorded. The present one was caused by a 6 m.m. calibre revolver bullet which entered the chest at the third intercostal space just beneath the third cartilage. The author describes the technique of the operation performed an hour after the injury was received. The patient recovered in ten weeks, and he reported himself well eight months after.

BRADYCARDIA IN INTESTINAL AFFECTIONS.

Maurice Loeper (*Presse médicale Belge*, November 9, 1913)

has seen bradycardia in many cases of gastric neuroses and ulcers, especially of the lesser curvature. Bradycardias are commoner in simple mechanical disturbances, or to discrete irritations of the intestine, enteritis, or lithiasis. He relates a case cured by severe regimen, of intestinal disinfection, hydrotherapy, valerian and belladonna. Sometimes, too, robust purgation is the determining factor in bradycardia. A case of Dr. Singer's is quoted in which the patient after three days' constipation took a strong purge, and felt pain in the head and syncope of forty minutes' duration with arrest of pulse and heart which beat only four to the minute. The patient recovered. The author describes two varieties of bradycardia : (1) The muscular, due to lesion of the bundle of His, and (2) The nervous, due to lesion or irritation of the vagus nerve. To the latter belongs the intestine. Rapid improvement sometimes follows two drop doses of Tr. belladonna. The vagus is involved in abdominal affections, sometimes by compression, inflammation, toxic impregnation, toxi-infection, or invasion of lymph nodes. The author thinks it possible that bulbar lesions, compressions of the vagus in the neck or mediastinum, or primary neuritis of the vagus may provoke simultaneously both bradycardia and intestinal reaction. He insists on the need for careful abdominal examination in all obscure cases of nervous bradycardia, also of the cardio-vascular system.

THE RELATIONSHIP OF PULMONARY TUBERCULOSIS IN CHILDHOOD (HILUM PHTHISIS) TO THE PHTHISIS OF ADULT LIFE, WITH A COMPARISON OF THEIR SYMPTOMS AND SIGNS.

By J. P. CULLEN, M.D.

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THE possible channels of infection in the *Phthisis of Adult life* are fairly well known, and may be classed in order of their importance as aerogenic, dietetic, and of more academic interest, inoculation and hereditary.

In Hilum Disease, in which X-ray examination shows the most obvious changes to exist at the roots of the lungs, viz., enlarged glands, matted or discrete, and coarse radiating striæ, with only in the later stages involvement of the lung tissue proper, the chief portals of entry are, as in the adult form, aerogenic and dietetic. Some confusion has, however, arisen as to the chronological order of events in the lungs and glands respectively, for which, perhaps, the use of the Röntgen rays is to some extent responsible, and a further consideration of these two methods of infection is necessary.

(1) *The aerogenic group*, due to inhalation of tubercle bacilli. As these germs are not endowed with mobility, it is necessary that they shall be taken up by leucocytes, and so carried into the lung tissue proper. Such leucocytes exist free in the alveoli, and Hamilton has shown that only in the alveoli can such infection take place, as the isolating properties of the basement membrane prevent infection in any other part of the air passages. Bacilli carrying leucocytes may come to rest and disintegrate in any part of their wanderings, either at the start giving rise to the terminal bronchiolitis which Rindfleisch has shown to be the commonest initial lesion in adult tuberculosis, in the course of the lymphatics, involving the vessel walls in a lymphangitis which shows itself under the X-rays as

an arborescent network of fine or coarse striæ, or finally in the meshwork of the lymphatic glands at the hilum of the lungs, giving rise to the opacities so common in this region.

(2) *Infection by the Alimentary Canal.*—While the relative importance of this method, as compared with (1), is still *sub judice*, certain facts admitting of very little controversy must be kept in mind. The lymphatics of the intestines end in the mesenteric glands; these again are in direct communication with the receptaculum chyli, and *viâ* the thoracic duct with the left subclavian vein. There is nothing to prevent tubercle bacilli travelling along these paths, and then, *viâ* the small radicles of the pulmonary artery, which, as Zuckerkandl has shown, supply the terminal bronchioles, infecting the lung tissue proper, and secondarily the lymphatics draining the infected area. Such lymphatic involvement is, however, always secondary, and the theory of Weleminsky (Weleminsky *zur Pathogenese der Lungentuberculose*), that the bronchial glands can be involved directly by infected lymph, received from the mesenteric glands, has been shown to rest on no anatomical basis. The bronchial glands are connected with the lungs, and are not the terminal reservoirs that Weleminsky asserts, and his views may be definitely ruled out of court.

The conclusions, therefore, arrived at are that, in both adult and infantile tubercle the path of infection is identical, in both it is at first pulmonary, and the point of entry is the vicinity of the terminal bronchiole. In the adult, possibly owing to blocking of the lymph paths by a previous lymphangitis—tuberculous or due to mechanical irritation, *e.g.*, dust—the bacilli at first remain localized to the neighbourhood of the point of entry, and a bronchiolitis and bronchopneumonia are produced, which undergo the usual changes of caseation, fibrosis, calcification, or softening. In childhood, the above agencies are not called into play to such an extent, so that the infection does not remain local, lymphatic involvement takes place, the glands and the lymphatics themselves in part or whole of their course are definitely infected. It is not necessary, in any case, to pre-suppose, as has been done, a retrograde flow of lymph, which is contrary to all anatomical teaching. The path of infection is always centripetal, and the symptoms and signs will depend on

where arrest of the bacilli occurs.

In the Adult type, this takes place at the beginning of its journey, leading to direct implication of a mucous surface. *Local Symptoms, e.g.*, cough, expectoration, hæmoptysis, are then those for which the patient usually seeks advice. *General Symptoms* make their appearance later on. *Physical Signs*, owing to the situation of the lesion, are sufficiently well marked to enable an early diagnosis to be made by the usual methods of inspection, palpitation, percussion and auscultation.

In Childhood, Local Symptoms are indefinite. There may be reflex cough and perhaps vomiting, attributed in some cases to irritation of the vagus. *General Symptoms are more marked.* The patient is languid, anæmic, perhaps suffers from night sweats or slight evening pyrexia, and growth and nutrition are interfered with. *Physical Signs*, owing to the depth of the lesions from the surface, are by no means obvious; enlargement of the oval interspinous area of dulness, with prominent venules over the region of the first to the fifth dorsal spines, crepitations in the nipple region, and harsh or cog-wheel sounds at the apices are the signs which suggest further examination, which is usually by means of the Röntgen rays, when the morbid appearance above mentioned may be disclosed. Pressure signs and symptoms occupy many pages in text-books; in practice, they may safely be disregarded.

Adult and Infantile Phthisis are therefore one and the same disease, the difference in their symptoms and signs are explicable on anatomical peculiarities. The affection in childhood may remain limited to the lymphatic paths, and in this case the prognosis is good, provided the disease is recognized early—in many cases, this can only be done by means of radiography—and treated by cod-liver oil and fresh air. Wrongly diagnosed, or diagnosed too late, the parenchyma of the lung is affected, and the case, perhaps comparatively late in life, passes into the adult variety, with far gloomier prospects of recovery.

THE GENERAL PRACTITIONER AND THE NEW BRITISH PHARMACOPŒIA.

By D. M. MACDONALD, M.D., F.R.C.P.

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THE year 1915 is responsible for the introduction of another British Pharmacopœia, a fact which cannot be ignored by the general practitioner. Whether the book is, or is not, an improvement on the 1898 and 1885 editions, is a question which might be answered differently by medical men and pharmacists. It would be useful and interesting to know on how many study-shelves the book might be found, and, indeed, equally so to ascertain the number of medical men who never see, or who never have seen this book.

A genuine regard for the British Pharmacopœia, on the part of the general practitioner, would most likely be regarded in these days as pathological. The link between the two is almost entirely one of dosage and the strengths of external applications; it is in order to emphasize certain changes in these, that this note has been written. It would be a palpable error to blame the average practitioner for his ignorance of standard preparations. Chiefly due to the hypertrophy of anatomy, the study of pharmacology is practically crowded out of his medical curriculum. As a result, the fifth-year student is lamentably ignorant of the subject, and, in consequence, of practical prescribing as well, so that his equipment comes to consist, in the main, of a superficial digest of his hospital pharmacopœia, and a list of compressed ready-mades with their actions and doses associated. His future in the realms of therapeutics may with safety be predicted.

Under the recent Insurance Act, this divorce from the book of official formulæ is likely to sustain a severe check. As is well known, there exists in many districts what is called an excess of prescribing. Close analysis of this reveals, too, on the part of certain prescribers, extensive ordering of proprietary articles which, owing to the necessity of widely advertising

them, really possess a fictitious value. In this connection, it may be well to state, that one result of the scrutiny of prescriptions will be to reveal the hitherto concealed weakness of prescribing on the part of a large body of men. Empirical prescribing will, on a large scale, assuredly receive a quietus.

It must be remembered that, on the Insurance Committees, chemists are well represented as well as financially interested, and these men are not slow—why should they be?—to expose the product of the prescriber's skill (on paper), and discuss it accordingly. That being so, the point scarcely requires to be laboured that an improvement on the present empirical basis of prescribing is inevitable, and it behoves the doctor to wake up and look to his laurels. In many cases, it will easily be proved that his prescribing excess is in inverse ratio to his knowledge of the drugs employed. Such practitioners really deserve to be penalized by their panel committee, and an injunction (with some well-deserved and standard exceptions) might with advantage be issued enforcing the use of the British Pharmacopœia and no other; or in other terms, that the component parts of his prescription shall be found between the covers of that book. This would constitute a rational and salutary measure; it would standardize prescribing, and ultimately deal with the inefficient training for this essential part of a medical man's equipment, which has already been referred to.

The more important changes in dosage of internal remedies and the altered strengths of external applications may be summarized as follows:—

INTERNAL REMEDIES.

	Dose.	Previous Strength.
Acetum Scillæ - - -	5–15 ℥.	Double.
Acid. Nitric. Dil. - - -	5–20 ℥.	Decreased, but dose the same.
Acid. Phosphoric. Dil. - -	Do.	
Acid. Sulphuricum Dil. - -	Do.	
Ferri Phosph. Saccharatus - -	1–3 grs.	New preparation.
Inject. Cocain. Hypoderm. - -	5–10 ℥.	Half.
Inject. Morphinæ Hypoderm.	Do.	Do.

INTERNAL REMEDIES—*continued.*

	Dose.	Previous Strength.
Inject. Strychninæ Hypoderm.	5–10 ♏.	New preparation.
Liq. Hydrarg. Perchlor.	3ss–3i	Weaker ; same dose.
Liq. Potassæ	10–30 ♏.	Do.
Pil. Phosphori	1–4 grs.	Half.
Spt. Ætheris Nitrosi	15–60 ♏.	Max. dose less.
Spt. Juniperis	5–20 ♏.	Double.
Syrupus Chloralis	3ss–3ii	Slightly stronger.
Syrupus Codeinæ Phosph.	Do.	Do.
Syrupus Ferri Iodidi	Do.	One-third less.
Tabellæ Trinitrini	1–2 tabs.	Do.
Tinctura Aconiti	2–5 ♏.	Double.
Tinctura Belladonnæ	5–15 ♏.	One-third less.
Tinctura Camphoræ Co.	3ss–3i	Opium 10 per cent. more.
Tinctura Colchici	5–15 ♏.	Half.
Tinctura Digitalis	Do.	Reduced 20 per cent.
Tinctura Nucis Vomicæ	Do.	Reduced to half.
Tinctura Opii	5–15 ♏. (rept.) 20–30 ♏ (sing.)	Increased 25 per cent.
Tinctura Opii Ammoniata	3ss–3i	One-ninth weaker.
Tinctura Picrorhizæ	Do.	New preparation.
Tinctura Strophanthi	2–5 ♏.	Four times more.
Trochiscus Acidi Carbolici	½ gr.	Half.
Vinum Antimoniale	10–30 ♏. 3ii–3iv. (emetic).	Slightly weaker.
Vinum Aurantii	—	Alcohol increased.

EXTERNAL APPLICATIONS.

Emplastrum Belladonnæ	Half.
Linimentum Hydrargyri	Three-fifths less of Hg.
Liq. Ferri Perchloridi Fortis	Less iron.
Ung. Acidi Carbolici	25 per cent. weaker.
Ung. Hydrargyri	Reduced to 60 per cent.
Ung. Hydrargyri Ammon.	Half.
Ung. Hydrargyri Composit.	Three-fifths strength.
Ung. Hydrargyri Subchlor.	Double.

New names have been coined for certain drugs, such

as Barbitone for Veronal, and Hexamine for Urotropine.

The chief additions are adrenalin, and its solution, a hypodermic injection of strychnine already mentioned, theobromine and sodium salicylate, known as diuretin, saccharated phosphate of iron, lactate of lime, and bromide of strontium.

The scruple is practically omitted, while the use of ʒi, which may be 60 grains, or a fluid drachm, is discouraged, and grains used where solids are indicated. Only average doses are given, so when potent remedies are prescribed, it is still advisable to mark the quantity with a cross, or initial it, for the guidance of the pharmacist, and to show that the large dose is intentional.

Practical Notes.

TREATMENT OF TETANUS BY BACCELLI'S METHOD.

Paul Sainton recently reported to the Paris Academy some results, obtained in the treatment of tetanus by this method, in the temporary hospital at Cherbourg. The patients were all wounded soldiers, and were exceptionally severe cases. With the treatment was associated the administration of large doses of chloral hydrate.

The method eventually adopted was to give each day two injections of from 40 to 50 c.c. of a 2 per cent. solution of carbolic acid, so that the daily dose varied between 1·60 and 2 grammes. The injection was given subcutaneously, and, when possible, above the site of the wound and in its neighbourhood. If this could not be done, the injection was made into the front of the thighs or on a level with the abdomen. In two patients the injections were continued for a month, the total amount of phenol given being 48 grammes in one case, and 88 grammes in the other. Locally, the injections caused no pain, but two patients had erythema, and a brawny infiltration of the tissues. At no time did any symptom of carbolic intoxication show itself, and the urine was free from the characteristic black tint.

The patients were kept isolated and very quiet, in half darkness. Morning and evening each received an enema containing from ʒiss to ʒii of chloral with one or two yolks of egg and ¼ litre of milk. Nothing by the mouth was given to those in whom spasms were set up by attempts at swallowing.

Out of 22 cases treated, six were cured of tetanus; but of these two died, one of gangrenous inflammation of the leg, and the other from broncho-pneumonia.

The conclusions drawn from the experiences are:—

1. The method of Baccelli's carbolic acid injections, combined with the administration of chloral, has an undoubted curative effect upon the evolution of tetanus.

2. Carbolic acid, introduced by subcutaneous and intra-muscular injections in 2 per cent. strength, is retained in the organism, and is only eliminated very slowly in the urine.

3. In order that the treatment may be of effect, it is absolutely necessary that it must be instituted at the earliest possible moment, and on the appearance of the first suspicious symptom, such as a localized contraction near the site of inoculation or even a slight dysphagia.

4. The treatment with chloral should always be adopted. It is essentially symptomatic treatment, but every patient with tetanus who sleeps is on the road to recovery.

Boquel, of Angers, reports favourably as well on this treatment. He obtained nine recoveries out of 24 cases. He considers that prognosis is determined in the first place by the length of incubation. Ten cases, in which the disease developed in from four to seven days after the wound, all died; whereas three cases, which only developed after the 20th day, all recovered. The cases which call for most attention are those developing from the 8th to the 15th day. Of 11 cases of this class, six were

cured. In the British hospital out of seven cases of the same sort, four recovered. The symptomatic treatment can be associated with the specific treatment by anti-tetanic serum without prejudice to either. For this, Boquel uses three drugs only; phenol, chloral, and morphia. Chloral is given by the mouth if possible, in the form of syrup, every two hours or every two and a half hours, so that a daily total amount of from 12 to 16 grammes is given. It is often necessary to resort to enemata, in which case 20 grammes is a suitable minimum dose.

Phenol is given, according to Baccelli's method, by subcutaneous injections of a 2 per cent. solution. Boquel gives an average dose of one gramme daily, varying this amount according to the gravity of the case, from 0·60 to 0·80 gramme up to 1·40 or 1·50 grammes. He gives two-hourly injections of 4 c.c. It appears to have a sedative effect, and several patients asked for it because it relieved their spasms.

These two drugs, if given as soon as the earliest symptoms—trismus or exaggerated reflexes—show themselves, will prevent the appearance of the crises, or lessen their frequency. But the danger of tetanus seems to be essentially in the crisis, and when that appears it must be stopped as soon as possible. Boquel finds that small doses of morphia are most serviceable: $\frac{1}{6}$th of a grain repeated several times during the day is usually enough for the purpose. In addition, doses of $\frac{1}{12}$th grain will relieve, for the moment, the dysphagia, retention of urine, and spasm of the anus.

Besides this symptomatic treatment by drugs, there are other essentials to be carried out. The patient must be kept free from all noise and excitement in a darkened room. He must pass urine freely, and have a regular action of the bowels. Boquel as a rule gives a litre of lactose-serum, 50 per cent, by slow rectal injection (Murphy's method), and the diuretic effect is generally excellent. He has never failed to give every day, as recommended by Baccelli, 20 grammes of sodium sulphate, either by the mouth or in an enema. It is sometimes necessary to use castor oil or purgative enemata. The patients require plenty of nourishment, for they become very exhausted and very anæmic. They can often drink in spite of the trismus, at least after being under treatment for a short time, and the dysphagia can be allayed by morphia. Treatment must not be stopped too soon. A patient can only be considered to be cured after a minimum of from three to four weeks.—(*Journ. de Méd. et de Chir. prat.*, 10 Oct., 14.)

TREATMENT OF CRACKED NIPPLES.

Rudeaux and Cartier recommend that the cracked nipple should be washed with spirit lotion, 1 in 20, after suckling, and that then one of the following should be applied with a camel's hair brush.

(1) ℞ Balsami Peruviani,
Tincturæ Arnicæ - - - - ana ♏ xl.
Aquæ Calcis - - - - - ℥ss.
Olei Amygdalæ dulcis - - - - ℥i.
Misce. Fiat pigmentum.

(2) ℞ Tincturæ Benzoini Compositæ,
Tincturæ Tolutani - - - - ana ℥ss.
Misce. Fiat pigmentum.

(3) ℞ Liquor Hydrargyri Perchloridi,
Glycerini - - - - - ana ʒss.
Misce. Fiat pigmentum.

(4) ℞ Sodii Biboratis - - - - - ʒii.
Tincturæ Benzoini Compositæ - - - ʒiij.
Glycerini - - - - - - ʒv.
Aquæ Rosæ - - - - - ad ʒij.
Misce. Fiat pigmentum.

5 ℞ Liquoris Hydrogenii Peroxidi (12 vol.) - - ʒij.
Glycerini - - - - - - ʒss.
Misce. Fiat pigmentum.

6) ℞ Extracti Cannabis Indicæ - - - - gr. xxiv.
Acidi Tannici - - - - - gr. xlv.
Glycerini - - - - - - ʒi.
Misce. Fiat pigmentum.

After the paint has been applied, the nipple is covered with gutta-percha tissue or sterilized gauze.

In some cases, it is better to make use of the following ointment :—

℞ Mentholis,
Stovainæ - - - - - ana gr. viiss.
Zinci Oxidi - - - - - - ʒi.
Tincturæ Benzoini Compositæ,
Paraffini mollis - - - - ana ʒiiss.
Liquoris Rosæ dulcis - - - ℥ij.
Olei Theobromatis - - - - - ʒi.
Misce. Fiat unguentum.

Plicque recommends the use of the following topical applications, which are non-toxic, and can therefore be applied before suckling.

(1) ℞ Ceræ Albæ,
Olei Theobromatis - - - - ana ʒij.
Liquoris Rosæ dulcis - - - - ℥iv.
Olei Amygdalæ dulcis - - - - ʒi.
Misce. Fiat unguentum.

(2) ℞ Cetacei - - - - - - ʒi.
Ceræ Albæ - - - - - - ʒiiss.
Olei Amygdalæ dulcis - - - ad ʒiv.
Misce. Fiat unguentum.

(3) "Cold Cream" (French Codex) freshly made.

(4) ℞ Zinci Carbonatis - - - - - ʒi.
Glycerini - - - - - - ʒi.
Paraffini mollis - - - ad ʒi.
Misce. Fiat unguentum.

It is advisable that all these preparations should be made in small quantities, and put up in collapsible tubes rather than in the ordinary

ointment-pots. Their freshness is better preserved in this way, which is a point of importance.

For more active applications, which can only be used after suckling, the following can be recommended:—

(1) Lotions of aromatic wine, either pure or diluted with boiled water, or a 1 per cent. solution of chloral hydrate in boiled water.

(2) Bouchardat recommends the Balsam of Chiron, which must be applied in very small quantity exactly on the fissure:—

℞ Camphoræ - - - - - - gr. i.
Balsami Peruviani - - - - - gr. v.
Anchusæ Officinalis - - - - - gr. vij.
Ceræ flavæ - - - - - - 3i.
Terebenthinæ - - - - - 3iss.
Olei Olivæ - - - - - - 3iiss.

Misce. Fiat unguentum.

(3) With similar precautions in use, preparations containing tannic acid are useful.

℞ Acidi Tannici,
Camphoræ - - - - - ana gr. xv.
Balsami Peruviani - - - - - 3ss.
Zinci Oxidi - - - - - - gr. xxx.
Glycerini - - - - - - 3iiss.

Misce. Fiat unguentum.

(*Journ. de Méd. et de Chir. prat.*, October 10, 1914.)

THE USE OF SALOL WITH LIQUID PARAFFIN.

F. Goldby, writing in the *Pharmaceutical Journal* (March 6, 1915), says:—

Shortly before the outbreak of war and the subsequent scarcity and rise in price of liquid paraffin, I had conceived the idea that this might be improved and made more useful in some cases by combining salol with the liquid paraffin and flavouring. This question is more of medical than pharmaceutical interest; but, on submitting the idea to several medical men, all agreed that such a preparation might prove very useful. As salol is perfectly soluble in liquid paraffin, and the latter passes through the system practically unchanged, this would seem to be an ideal method of exhibiting salol as an intestinal antiseptic combined with the lubricating and laxative properties of the paraffin. I have been unable to find any previous reference to the use of such a preparation, and make the suggestion for what it may be worth. The formula I have employed is as follows:—

Salol - - - - - - 800 grains.
Oil of cinnamon - - - - 40 minims.
Chloroform - - - - - 4 fl. drachms.
Biebrich scarlet - - - - ½ grain.
Liquid paraffin - - - to 80 fl. oz.

Reviews of Books.

Lead Poisoning from the Industrial, Medical, and Social Points of View. By Sir Thomas Oliver, M.A., M.D., F.R.C.P. Pp. 294. London: H. K. Lewis. 5s. net.

Whilst the authoritative character of this work must attract readers with the most diverse interests, it will specially appeal to medical men, for the subject is approached mainly from their point of view. Historical and trade references, appropriate to a larger treatise, are here presented briefly, and in such a way as to bear on practical medicine. Many important questions, such as the *rôle* of peat and micro-organisms as lead solvents, are fully discussed in the light of most recent knowledge, whilst the value of blood-pressure in prophylaxis, of basophilia in diagnosis, and of de-ionization (a reversal of ionization) in treatment at once proclaim the modernism of its researches. Of the merits of electrolysis as a lead eliminant, the author speaks in no uncertain voice, and his opinions should eventually lead to its general adoption by medical practitioners, and possibly by employers themselves. The pernicious effects of lead on fecundity, both in males and females, is presented in a complete and convincing manner. One would have welcomed suggestions as to how its criminal use could best be suppressed, but it is possible that the author regards this as beyond the purview of his lectures, or that he hesitates to trespass far into the domain of State medicine. It is obvious from the text, although not expressly advocated, that the compulsory notification of *all* still-births and of *all* cases of plumbism could not fail to secure more effective recognition, not only of the prevalence of criminal abortion, but of the only too frequently undiscovered presence of lead in beer and other beverages, in foods and quack medicaments. Many medico-legal puzzles are dealt with, and solved in a delightfully luminous manner, among which may be mentioned the significance of Burton's line, of lead in the viscera and excreta, and the relation between lead absorption and legally accepted lead poisoning.

A timely note of warning is issued against the attempt by novices to conduct chemical analyses in these and kindred cases.

Finally, a sixty-page appendix setting forth the Factories and Workshops Orders *re* Lead, and a comprehensive index tend further to render this volume an indispensable addition to the medical bookshelf.

The Infant. By Eric Pritchard, M.D., M.R.C.P. London: Edward Arnold. 3s. 6d. net.

In the preface to this volume, the author explains that it consists of a series of lectures which have been given mostly at the Queen's Hospital for Children, and that these lectures have been edited for the present purpose. The book, as it stands, presents a review of the author's views on the subject of infant feeding, and does not attempt to enter into the details of the feeding of individual cases, rather dealing with main principles. The author says that his views may seem to some revolutionary and unorthodox, but for the most part they appear to us to be characterized by a robust

common sense, and an insistence that no infant can be fed by a strict adherence to rules laid down on broad general lines. In addition to the chapters on the feeding of infants, there are others on closely allied subjects, for instance, rickets and convulsions. In these, as in the other parts of the book, Dr. Pritchard shows that he can think for himself and free himself from the mere traditional views of the disease. A short notice is not the proper occasion to attempt any detailed criticism of an author's opinions, and we will only say here that it appears to us that, in a few instances, Dr. Pritchard has somewhat overstated his case, and that the argument would gain in cogency, if it were put in a rather less controversial manner. The reader will rise from its perusal with a fresh light upon many points in an extremely difficult matter, and with a respect for the resolution with which the author has grappled with the problems. The volume shows all the evidence of care in production, which the medical profession has learnt to expect from the house of Edward Arnold, and it will enhance the reputation of its author already so deserved.

A Text-Book of Practical Therapeutics. By HOBART AMORY HARE, M.D., B.Sc. Fifteenth Edition. Enlarged, thoroughly revised, and largely re-written. Pp. 998. Illustrated with 144 engravings and 7 plates. London: Henry Kimpton. 21s. net.

A PERUSAL of Part I., "General Therapeutical Considerations," will show the enormous advance which has been made in the scientific treatment of disease, since the first edition appeared in 1890, and it is the special merit of the book we have before us that the author is well abreast with all the most recent additions which have been made to therapeutics. He puts this point very well, when he says that the advance has been "from pure empiricism into scientific accuracy."

The book, which is most conveniently arranged for reference, is divided into four parts. Part I., as already mentioned, is devoted to "General Therapeutic Considerations." Part II. gives an account of drugs, their physiological action and therapeutics. Under this heading is included the incompatibility of the drug in question, any untoward effects which have resulted from its administration, and the best way of prescribing it. Part III. is concerned with remedial measures, other than drugs, and foods for the sick. This is certainly one of the most valuable sections of the book, for it gives a full account of the various methods of treatment, from those, such as bleeding and cupping, employed by our forefathers, to the most modern methods, as lumbar puncture, kataphoresis, and vaccine therapy. We have carefully examined the directions given for carrying out the various procedures recommended, and we can vouch for the ability and thoroughness with which they are described. In the section devoted to transfusion, the author insists that the ordinary solution of common salt in distilled water may be harmful in certain conditions, and he maintains that the best solution for transfusion is the following:—

Calcium chloride - - - -	0·25
Potassium chloride - - - -	0·1
Sodium chloride - - - -	9·0
Sterilized water - - - -	1,000 cc.

Part IV. gives in alphabetical order the principal diseases and their

appropriate treatment. In discussing migraine, no mention is made of the fact that it is often associated with high tension, especially at the menopause, and in this case the administration of iodide of potassium, with or without bromide, in the intervals has usually a most satisfactory effect. The book concludes with a list of doses, a good index of drugs, remedial measures, and diseases.

The fact that the book we are considering is the fifteenth edition is a conclusive proof of the estimation in which it has been held in the past, and we can most warmly recommend it to our readers as containing in a convenient and practical form all that need be known of the treatment of disease.

Obiter Scripta, Throat, Nose, and Ear. By A. R. Friel, M.A., M.D. Pp. 40. Bristol: John Wright and Sons. 2s. 6d. net.

A small brochure of three chapters, dealing, in a "chatty" way, with miscellaneous points on common conditions of the throat, nose, and ear; zinc ionization in suppurations in the middle ear and nasal accessory cavities; and the treatment of ozœna.

It contains several useful hints, and is well worth reading.

Essentials of Physiology. By F. A. Bainbridge, M A., M.D., D.Sc., and J. Ackworth Menzies, M.D. Pp. viii. and 434. London: Longmans, Green & Co. Price 10s. 6d. net.

This book is a recent addition to the well-known "Essentials" series. Its object is to bring together in a concise form the fundamental facts and principles of physiology, primarily with the object of meeting the requirements of the medical student preparing for a pass examination in the subject of Physiology. We think that the authors have well fulfilled this task, and in addition the practitioner, who desires to refresh his memory and to obtain an idea of the latest developments of physiology, will find this book an excellent one for the purpose. The chemistry of the body is well done, and the chapter on the central nervous system gives a clear account of this difficult subject. The polymorphonuclear leucocytes are stated to be *neutrophile*, they are strictly jointly *acidophile*. The chapters on metabolism, food and diet, give a capital summary on these subjects. A chapter is devoted to the important subject of the ductless glands. Details of histology are omitted, for this is dealt with in another volume of the series. The book is profusely illustrated, and the many tracings inserted are most useful. Altogether we can confidently recommend this book.

A Text-Book of Surgery for Dental Students. By G. Percival Mills, M.B., B.S., F.R.C.S., and Humphrey Humphreys, M.B., Ch.B., B.D.S., L.D.S. Pp. 340. Illustrated. London: Edward Arnold. 12s. 6d. net

The book is written solely for students and practitioners of dental surgery, and is modelled on the new curriculum of the Royal College of Surgeons of England. It is claimed also that it includes all the requirements of the various licensing bodies both in this country and in America. The larger part of the book is devoted to general surgical pathology, and

the chapters on this subject are clearly and succinctly written, but might, with advantage, have been illustrated more often by reference to mouth conditions.

The authors do not appear to attach sufficient importance to oral sepsis; as a cause of chronic inflammation of the bones of the jaw, of chronic pharyngitis, or of chronic glossitis, it receives no mention. Gout is credited with producing inflammatory exostoses of the mandible. The authors appear to take the view that the chest deformity of adenoids is due to the child's inability to take a deep inspiration, so that the lungs do not expand properly, this being followed by flattening of the chest and drawing in of the ribs. Obviously, the child has only to open its mouth to obviate all deformity, if this were its genesis. The pages on antral suppuration are not up to the general standard of the book.

If the dental student wants his surgical pathology and his regional surgery brought together in one volume, the present volume may confidently be recommended to him; but it must be acknowledged that there is little in the regional surgery of the book, that will not be found in the current text-books on dental surgery.

Diagnosis in the Office and at the Bedside. By HOBART AMORY HARE, M.D., B.Sc. Pp. 547. London: Henry Kimpton. Seventh Edition. 18s. net.

THE book before us will appeal to every practitioner of medicine, who is in doubt as to the precise significance of any particular symptoms. As the author points out in the preface, the symptoms used in diagnosis are discussed first, and their application to determine the character of the disease follows. Every symptom is carefully considered from all points of view, and the diagnosis is arrived at by the grouping of symptoms. In this way, the author follows the method which should be employed in practice. The introduction on general diagnostic considerations deserves attentive reading. At the present time, there are so many instrumental and laboratory aids to diagnosis, that there is a danger lest the student should neglect the thorough and systematic examination of the patient by his unaided senses. The great physicians of the last century arrived at their diagnosis with but little outside assistance, and it is to be hoped that the present generation, while rejoicing in many methods of investigation unknown to their predecessors, will also cultivate their skill in facial and symptomatic diagnosis.

The book is illustrated with 165 engravings and 10 plates, which are of great assistance in elucidating the text. We would also comment on the number of valuable tables of differential diagnosis, many drawn from various authors, but some are original. Diagnosis has evidently always been a strong point with the author, as is shown by the fact that, as long ago as 1888, he obtained the Fothergillian Prize of the Medical Society of London for his essay on "The Pathology, Clinical History, and Diagnosis of Diseases of the Mediastinum."

We must now draw attention to some of the omissions we have noticed in the book. In describing the methods employed in testing for knee jerk, no mention is made of the plans of reinforcement, devised by Jendrassik and Laufenauer. In the descriptions of the results obtained on auscultation,

bronchophony is alluded to but not described, though pectoriloquy and ægophony are both described. There is also no reference to the zone of enlarged venules along the line of the attachment of the diaphragm which is so commonly seen in emphysema, and occasionally met with in other conditions. We would comment as well on the omission to mention the diastolic thud, or shock, as a diagnostic point of great value in the recognition of aneurysm in the first and second parts of the arch of the aorta.

In another edition, the author will probably allude to the curious attacks of pyrexia, which occasionally follow a rat bite. The index appears very complete, but the first symptoms, Stellwag's, we looked up were wrongly indexed! In spite of omissions, the book is one which we can most warmly recommend. It is admirably printed and illustrated, and we can conceive of no greater assistance to the busy practitioner who has a puzzling case under observation.

Diseases of the Ear, Nose, and Throat. By GEORGE NIXON BIGGS, M.B., B.S. With illustrations. Pp. 477. London: Oxford Medical Publication. 10s. 6d. net.

THIS book is written, as stated in the preface, to meet the needs of a busy general practitioner. The omission of pathological and anatomical details does not detract from its value in fulfilling the above purpose, but renders it easier reading. The striking feature is the unusually elaborate system of diagnosis and differential diagnosis, which is fully given with each disease, even at the expense of some repetition, but on the whole it is quite good and likely to prove most useful.

Treatment is dealt with rather more clearly and definitely than in many books on the subject, is described in detail, and a list of useful formulæ is included in an appendix. Alternative methods are not elaborately given. Some few plates are reproduced from photographs, but the greater part of the illustrations are rather crude diagrams, which are not pleasing at first sight, but will be found most usefully descriptive when reading the subject matter. We would particularly indicate as meriting careful study, the tabulated accounts of the clinical tests for the various forms of deafness which are often so confusing to the beginner yet so valuable to the expert. The diagnosis and differentiation of the intracranial complications of otitis is given in an article, which we consider one of the best we have read.

The list of operations, recommended as within the scope of the general practitioner, is rather generous, and we think would require some study in a special clinic for their accurate performance. The description of the operations is rather meagre, but good. On the whole, the book is reliable, readable, and well-planned, and will repay careful study by all in general practice, and advanced students.

X-rays; an Introduction to the Study of Röntgen Rays. By G. W. C. KAYE, B.A., D.Sc. Pp. 252. London: Longmans, Green & Co. 5s. net.

THIS is an attractively got up book, written by a physicist mainly for physicists; but the author rightly "trusts that the form of the book will be acceptable particularly to the members of the medical profession,"

in view of the further possibilities "of the rays which Röntgen has placed at their service." He deals in a natural and logical succession with the phenomena of the discharge tube, cathode rays, X-rays generally, the X-ray bulb, the means of the excitation thereof, its hardness and its blackening, the measurement of X-rays, secondary X-rays, ionization, practical applications of X-rays, their interference and reflection, and finally on their nature. Among the appendices is a full account of Coolidge's X-ray-bulb with its hot (Tungsten) spiral filament cathode.

Here criticism must be confined to the chapter on the practical applications of X-rays; this is all too brief. It contains no reference to the subject of radiographic perspective, which if made by a physicist would have great weight with the physician. The X-ray prints on p. 155 and elsewhere are printed over their backs, rendering it impossible to view them from their proper side; these pictures cannot, therefore, conveniently be brought to lie "in perspective" with the objects from which they were taken. The (doubly printed) "plastic print" on page 162, picturesquely simulating a low relief, is of course quite illusive. Analogous to the "facia" writing of a shop front, it is very pretty, but does not correspond to the real relief of the original objects; as the author puts it, it is "pseudo-relief."

The numerous illustrations and tables are *à propos* and convincing There is a careful and full index. We strongly recommend this interesting, comprehensive, and thoroughly modern book.

Public Health Laboratory Work. By HENRY R. KENWOOD, M.B., D.P.H. Sixth Edition. Pp. xii. + 418. London: H. K. Lewis. 10s. net.

THIS book is so well known and has found such favour with students, that there is little need to do more than direct attention to the appearance of this sixth edition. The principal change from its predecessors consists in the exclusion of almost all matters relating to bacteriology, thereby keeping the volume within compass as a handy laboratory guide to the chemical side of public health laboratory work.

We find that references to recent work have been freely included; for instance, the *Lancet* method of examining air for the products of combustion of gas-stoves, phosphuretted hydrogen which may be generated from ferro-silicon, bean or synthetic milk, the relation of "polished" rice to beri-beri, etc The descriptions of analytical methods are always clear, and the worked-out examples appended are useful additions.

An Introduction to the Study of Infection and Immunity, including Chapters on Serum Therapy, Vaccine Therapy, Chemotherapy and Serum Diagnosis, for Students and Practitioners. By CHARLES E. SIMON, B.A., M.D. (Baltimore, U.S.A.). Second Edition. Pp. 325 With 11 plates and 18 illustrations. London: Baillière, Tindall & Cox. 14s. net.

So much interest is taken in the subject of immunity, which, in its modern connotation, implies almost everything of real importance in connection with the prevention and treatment of infectious diseases, that it is

a matter for congratulation that works such as these are published, which enables the busy practitioner to keep abreast with the rapid march of modern knowledge. This book is an excellent example of its sort, but in writing such a book there must be great dangers in excess or in defects. Either the work must stretch to an unwieldy length, so as to become a work of reference only (in which case it must soon become obsolete), or it must pass over in silence facts and theories of great importance. Dr. Simon has escaped both these dangers very creditably. The book is not too long to be read with unflagging interest, but it gives a very fair account of almost everything of prime importance. The chapters on anaphylaxis, in which special care is taken to point out the clinical importance of the phenomenon, on serum treatment, chemotherapy, and on the serum diagnosis (which includes an account of the Abderhalden test for pregnancy) are especially commendable.

Tuberculosis of the Bones and Joints in Children. By JOHN FRASER, M.D., F.R.C.S.E., Ch.M. London: A. and C. Black.

THIS handsome volume, appropriately dedicated to Mr. Stiles, forms a comprehensive account of the present views on the surgery of tuberculosis of bones and joints and of the methods of treatment in vogue in Edinburgh. It is divided into two main parts: that dealing with the general aspects of the subject, and that dealing with tuberculosis of particular bones and joints. It is well illustrated with a profusion of drawings, micro-photographs, diagrams, and a few coloured prints. Most of these leave little to be desired, but the reproduction of the X-ray photographs are unsatisfactory. These are so reproduced as to leave the impression that they have been rather extensively "touched up," in order to display the points to which the author desires to draw attention. If this be so, we would suggest that either the original radiograph or a frank diagram based on it is preferable to a reproduction which is neither one nor the other.

The book is strong on the pathological side, and the author is fully entitled to ask us from his own work to accept some of the conclusions which he promulgates. His micro-photographs in this part of the work are especially good and to the point, and the net result is to set forth an account of the pathology of bone tubercle, which is unusually clear and convincing. Symptoms are dealt with in a general section, as is also treatment. This completes the first part of the volume, the second half of which is reserved for the more detailed consideration of the special bones and joints. The bulk of this part is devoted to the spine and the hips, but even the most unusual sites receive adequate attention and illustration.

Anyone who is concerned with the treatment of tuberculous children, naturally turns at once to the section dealing with the question of tuberculin. The author is, perhaps, not sufficiently dogmatic on this point, but we gather that he prefers not to allow any means of treatment to be neglected, while believing that tuberculin inoculation in itself is not of much advantage; he appears to favour the employment of injections controlled by opsonin estimation, a method which is quite impossible for the great majority of medical men who have to treat bone tubercle.

We congratulate the author on a book, representing an amount of

hard labour, which it is difficult for the casual reader to appreciate, the publishers on the appearance of the volume, and the Royal Hospital for Sick Children, Edinburgh, on the presence of Dr Fraser on its staff.

Meningococcus Meningitis. By H. Heiman, M.D., and S. Feldstein, M.D. With introduction by H. Koplik, M.D. Pp. xiv + 307. London: The J. B. Lippincott Co. 12s. 6d. net.

The appearance of this monograph does great credit to Mount Sinai Hospital, and to the organization and thoroughness of its pædiatric department, which is under the control of Dr. Koplik. It forms a modern, trustworthy, and exhaustive guide to all that is known, at the present time, of the bacteriology, epidemiology, clinical course, and treatment of a disease now thoroughly well-known, at least to all children's physicians in the civilized world. The history of the disease begins in the early part of the 19th century, and, clinically, it was fairly well recognized in most of its manifestations by the middle of the century; but it was not until 1887, that the organism of the disease was discovered by Weichselbaum. It was only in the last decade of the century, that the researches of other bacteriologists fully confirmed Weichselbaum's announcement, and that the sporadic form of the disease was, thanks to Still and others, fully recognized as a form of the epidemic affection. It was left for the 20th century to take the next great stride, the elaboration of a serum which should be able to control the manifestations of the disease, at least in some degree. In this triumph, the American Flexner has won the largest share.

The volume under notice recounts the details of this interesting story, and surveys in successive chapters the bacteriology, the epidemiology, the modes of dissemination so far as they are known, the morbid anatomy, the clinical types of the disease, the diagnosis, and the treatment. In every chapter there is a fund of information, and we have not been able to find any material point unnoticed. Perhaps the authors lay less stress than English writers usually do, on the frequency of that curious transitory blindness: it is mentioned, and as being more frequent in the infantile form of the disease, but they add that, fortunately, it is rare. The reviewer believes that, in the infantile cases seen in this country, it is a frequent phenomenon, and one of very considerable value in diagnosis. A valuable point on which the authors insist is the comparative frequency of serum disease, which is said to occur in one-third of the cases treated. They refer on the authority of Levy to a fatal case. The charts and illustrations are well chosen and clear, and are refreshingly few in number, being used only to demonstrate those points which lend themselves to this method. The index is the only weak point in the book; we have tested it, and found it deficient in many items, while in others it is over rich in references and cross references. But this defect, though irritating, is not important, and we repeat that the volume is, in all other respects, a model of what such a monograph should be.

Preparations, Inventions, etc.

SOME IMPORTANT MEMORANDA FOR THE BUSY PHYSICIAN.

(New York: The Fellows Medical Manufacturing Co., Limited, 26, Christopher Street.)

In reading current medical literature, it has become more and more difficult for the busy practitioner to remember at the moment what is implied by "A's syndrome," "B's sign," "C's test," *et hoc genus omne*. This pamphlet contains a concise description of those most commonly in use, and is a welcome help in the trouble caused by this most unsatisfactory method of labelling.

"TABLOID" WATER STERILIZER; "SOLOID" POTASSIUM IODIDE AND STARCH.

(London: Messrs. Burroughs Wellcome & Co., Snow Hill Buildings, E.C.)

These preparations present a new method for the rapid sterilization of water for drinking purposes. The process is quicker and more convenient than sterilization by heat, and can be depended upon to free contaminated water from living organisms, including those of typhoid and cholera, as well as those causing dysentery.

Sterilization is effected by means of chlorine, set free in the water from chlorinated lime. The free chlorine is then eliminated by means of sodium thiosulphate. The issue of these substances in tabloid form has greatly simplified the method, for it can be put into practice anywhere, in the field or in camp, without requiring the help of weights and scales.

The unit adopted is 10 gallons of water. To this quantity, one "tabloid" chlorinated lime, reduced to powder, is added, and mixed thoroughly with the water. After standing for 15 minutes, the water is then tested for chlorine. This is done by taking a little of the water in a cup, or other vessel, in which has been placed a "soloid" potassium iodide and starch. The presence of free chlorine is shown by a blue colour, and proves that sufficient chlorinated lime has been used.

If, however, this test is negative, more chlorinated lime is required to complete sterilization, and a second "tabloid" is added to the water. After 15 minutes, this is tested again, and the process must be repeated, if necessary, at intervals of 15 minutes, until the blue colour appears in the test. The sterilized water is then freed of chlorine by means of the "tabloid" sodium thiosulphate. One of these is dissolved in an ounce of the water, and this solution is thoroughly mixed with the bulk of the water. This will then be found to have had all taste of the sterilizer removed, and is ready for drinking.

"Tabloid" water sterilizer is issued in cartons containing one bottle of 25 "tabloid" chlorinated lime, and one bottle of 25 "tabloid" sodium

thiosulphate. The "tabloid" potassium iodide and starch is issued in bottles of 25.

SAL HEPATICA.

(New York: The Bristol-Myers Co., 277–281, Greene Avenue, Brooklyn, U.S.A.)

This preparation is a combination of salines with sodium phosphate, and is effervescent. When mixed with water, an artificial mineral water is produced, which is more palatable than many of the natural "bitter waters." It should be given with plenty of water, hot or cold, but not iced. It is stated that it does not cause griping, and is recommended for use as a safe and reliable laxative.

PATENT PRESCRIPTION WALLET.

(London: Messrs. M. Bresillon & Co., 9, Gamage Buildings, Holborn, E.C.)

This is a very well got-up and useful prescription wallet, which will be supplied, free of all charge, to those members of the Profession writing for it, and mentioning THE PRACTITIONER. The wallet contains a celluloid tablet for memoranda, in addition to the most ingenious arrangement conceivable for prescription sheets. We advise our readers to write for the wallet, and we understand that Messrs. Bresillon will also be prepared to supply, free of charge, prescription sheets (printed with the name, address, telephone, etc. of the prescriber) suitable for use with the wallet.

THE PRACTITIONER.

MAY, 1915.

THE TREATMENT OF CEREBROSPINAL MENINGITIS (SPOTTED FEVER).

By SIR WILLIAM WHITLA, M.A., M.D., LL.D.

Professor of Materia Medica and Therapeutics, Queen's University, Belfast; Senior Physician, Belfast Royal Hospital; Examiner Indian Medical Service, etc.

In view of the prevalence of cerebrospinal meningitis at the moment, the Controlling Editor of THE PRACTITIONER has asked me to contribute a short article on its treatment, with which request I have much pleasure in complying. The following notes are substantially taken from my *Dictionary of Treatment*, but I have revised them, so as to include the latest information obtainable on the subject.

ACUTE CEREBRAL MENINGITIS OF CHILDHOOD.

Confining this title to the simple non-suppurative inflammation of the pia-arachnoid, involving chiefly the base of the brain, which is synonymous with posterior basic occlusive meningitis, the treatment indicated is that common to all forms of cerebral leptomeningitis.

Absolute rest in a cool, darkened, and thickly-carpeted room, shut off from noise and all source of vibrations, is essential. The child may be kept on the lap of a reliable nurse, with the head kept slightly elevated, when rest in bed is not tolerated. An ice-cap or Leiter's tubes should be kept continuously in contact with the scalp.

Dietetic considerations are of more importance in the management of this type of cerebral meningitis than in the other varieties, since the affection often runs a chronic course, and the maintenance of life may ultimately depend upon the successful administration of food from the onset. Hence, small quantities of diluted milk or suitable infant food should be administered assiduously at short intervals, and resort to early rectal feeding may be required if the stomach is irritable; strong soups or animal food in any form should be prohibited.

A smart purge, 1 gr. Calomel or 2 grs. Hyd. cum Creta given in a teaspoonful of Syrup of Senna, may be administered

in order to evacuate the bowels thoroughly.

The treatment must be mainly symptomatic; cephalalgia and restlessness may be relieved by bromides, with 1 or 2 grs. antipyrine added to each dose. Leeching of the temples and a mustard poultice to the nucha often afford considerable relief.

Vomiting may be controlled by rectal feeding and a sinapism over the epigastric region; the latter agent is more suitable for the relief of vomiting of gastric origin, but it occasionally answers in cerebral irritation.

High temperature must be treated by patient, tepid or cold sponging, and sleeplessness, which does not yield to bromides, should be relieved by a small dose of chloral.

Lumbar puncture is a valuable agent for the relief of most of the urgent head symptoms, but it is more clearly indicated in the later stages when accumulation of effused inflammatory products are causing increased cerebral pressure.

Although simple acute basic meningitis is widely accepted as being a sporadic form of epidemic cerebrospinal meningitis, and due to the presence of the *Diplococcus intracellularis*, information is still lacking of the value of intraspinal injections of Flexner's serum in the simple type. The researches of Houston and Rankin have demonstrated that the coccus found in the simple basic type differs in its opsonic and agglutinative reactions from the coccus found in epidemic cases. Nevertheless, in the opinion of the writer, the serum should always have a fair trial in every sporadic case in which the diagnosis of tubercle can be excluded, especially as it appears that its injection cannot do harm, if the cerebro-spinal fluid be first permitted to drain away through the needle before injection.

Recently, urotropine has been extolled for its antiseptic action; it may be given by the mouth, but there is no proof that it has any effect.

As the accumulation of the inflammatory fluid products in the cerebral ventricles leads to their distension, owing to blocking of the iter and the openings from the fourth ventricles, hydrocephalus is liable to supervene. Lumbar puncture is clearly indicated at this stage, though its effects are usually but temporary.

Incision of the tympanic membrane on both sides sometimes affords marked relief to pressure symptoms, and it should

always be resorted to where there is any otitis present.

Mercury unquestionably is of great value in aiding the absorption of the effused liquid, but it must be pushed by inunction till its physiological effects just begin to show themselves. This should be resorted to in every case of simple meningitis. The writer has so many times witnessed most striking recoveries from full doses of the metal by the skin, after profound coma had almost obliterated all hope of improvement, that he believes it to be unjustifiable to abandon the patient to his fate without resorting to vigorous treatment by this drug. Iodides may be employed alone or in conjunction with mercurial treatment.

When chronic hydrocephalus follows and the case does not yield to lumbar puncture, little permanent good need be expected by tapping the ventricle with a fine needle, introduced outside the longitudinal sinus through the anterior fontanelle. The only procedure from which any lasting benefit may be expected is drainage of the lateral ventricle by the introduction of a fine tube of gold, bent suitably so as to reach the descending horn of the cavity ; the upper extremity of the tube is to be fastened by sutures to the dura mater on its smooth internal aspect. By this operation, the fluid in the interior of the distended cerebral cavities is brought into direct communication with that in the subarachnoid space.

The term *chronic* meningitis is sometimes applied to the cases of simple basic meningitis which run a slow course of months, and these are identical with those somewhat rare examples of cerebrospinal meningitis, in which the same obstructive factors are at work inducing acquired hydrocephalus, by obliterating the passages between the ventricles and the posterior lymph cistern. The only treatment from which any permanent benefit can be expected, after the failure of mercury and iodides, lies in the drainage of the ventricles.

The *acute idiopathic internal hydrocephalus of Quincke*, being due to a chronic inflammatory condition of the lining membrane of the ventricle with serous accumulation and no blocking of the iter, yields to lumbar puncture in conjunction with mercurial treatment.

CEREBROSPINAL MENINGITIS (EPIDEMIC).

This affection is also known as spotted fever and as cerebrospinal fever, and, as already stated, is regarded as the epidemic

form of the sporadic disease.

The treatment is to be conducted upon the lines laid down for the management of simple basic meningitis. Rest in a darkened room, with the head elevated and ice applied to the shaven scalp, are clearly indicated. The cerebral symptoms—cephalalgia, restlessness, insomnia, etc.,—call for palliatives, such as bromides, antipyrine, and an occasional dose of chloral or trional. Leeching behind the ears or over the occiput may be employed; mustard to the nucha or the application of the ice-bag to the spine may afford relief to the acute spinal symptoms. Blistering over occiput or nucha should never be employed owing to the danger of sloughing. Morphia, though generally contra-indicated in other forms of meningitis, may safely be employed to relieve violent spinal pain, and is especially indicated hypodermically, when the vomiting is uncontrollable by other methods. Fever should be reduced by continuous cold sponging, or, in the case of children, by tepid bathing.

No drug possesses any specific action upon the growth and development of the *Diplococcus intracellularis*, but unquestionably a valuable agent lies in the serum of Flexner, and many lives in recent epidemics have been saved by its use. Thus, in the Belfast epidemic of 1906–1908, Robb reduced the mortality from 74 to 30 per cent. after failing to influence the death-rate by the use of the sera of Ruppel, Kolle and Wassermann, or Burroughs and Wellcome. More recently Robb has published a further 117 cases with only 28 deaths, which represents a further reduction of the mortality to 24 per cent.

As in the employment of serum therapy in other microbic diseases, such as diphtheria and tetanus, the "time" element is the vital factor in obtaining the best results. Thus Flexner's serum should be resorted to at the earliest possible moment after the diagnosis has been established, and, during an epidemic when suspicious symptoms are met with, it may be advisable not to lose time by a bacterial investigation or by a determination of the opsonic or agglutination tests, but to inject the remedy without delay.

Lumbar puncture under anæsthesia by chloroform having been performed, and as much of the spinal fluid permitted to escape as will spontaneously flow through the needle, 20 to 30 c.c. of the serum, at a temperature of 100° F., should be

injected slowly by gravitation; a gentle pressure of the piston towards the end of the process may be necessary to inject the last portion of the dose. The injection should be repeated in 6 or 8 hours, if the spinal serum has been noticed to be purulent; a dose every day or every second day for six or seven times may be necessary in severe cases. Mild cases will be met by one or two injections. Acute fulminating examples of the disease terminate sometimes in a few hours, and will probably prove invulnerable to the serum, but when possible they should have the advantage which the serum alone holds forth.

Much has been written regarding the advantages of simple lumbar puncture in cerebrospinal fever. Some cases unquestionably have been markedly benefited by the operation in the acute stages, but upon the whole any real permanent benefit from its repeated use is only obvious in the later stages of the disease when the accumulated fluid is causing pressure within the cranium.

Where acquired hydrocephalus has commenced to manifest its presence, through blocking of the communications between the interior of the ventricles and the posterior lymph cistern, lumbar puncture cannot be expected to exert any but the most temporary relief. At this period, after the cessation of fever and toxæmia, a trial of mercury and iodides is clearly indicated, and, as in the hydrocephalus which follows simple basic meningitis, when these agents fail, resort to drainage of the ventricles as described in the preceding article should be gravely considered.

Prophylactic Treatment.—Of preventive measures nothing of any value is really known, since it remains to be discovered by what route the coccus gains its entrance to the body. There are serious doubts about the truth of the hypothesis that it enters through the nasal mucosa.

The organism, demonstrated by Symmers and Wilson in the water-supply during the Belfast epidemic, should suggest sterilization of the milk and water. There is no evidence that the disease is infectious or contagious, in the ordinary sense in which these terms are employed. Flexner's serum is almost certainly a prophylactic, but the suggestion of making a spinal puncture and injection for this purpose must be considered as Utopian. The serum is not to be relied upon as a curative agent when administered hypodermically like the other sera used in medicine.

CEREBROSPINAL FEVER.*

SYMPTOMATOLOGY AND DIAGNOSIS.

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[With Plates XLI.-XLII.]

GENERAL.

Definition.—A specific disease, due to infection of the body by the meningococcus, occurring both in epidemic and in sporadic form, and most often showing itself as an acute meningitis tending to involve the whole cerebrospinal axis.

The Causal Micro-organism.—The meningococcus (diplococcus meningitidis intracellularis) is a paired coccus, largely intracellular when observed in an inflammatory exudate, Gram-negative in its staining reaction. Although its viability outside the body is slight it is not difficult to cultivate, and with care it is readily distinguished in the laboratory both from micrococcus catarrhalis and from the gonococcus—the other two pathogenic micro-organisms which do not retain Gram's stain.

Mode of Entrance into the Body.—Although some doubt still exists on this point, it is extremely likely that the coccus is conveyed directly from person to person, most often by droplets of saliva in the course of conversation, coughing and sneezing, or by actual contact. The frequent incidence of the coccus in the pharynx both of patients suffering from the disease, or of persons with nasal and pharyngeal catarrh, and of healthy persons in an epidemic zone, suggests most strongly

* This name is preferable to "cerebro-spinal meningitis," because actual meningitis may not be present, or may not constitute the main lesion; but also because cerebrospinal meningitis may occur as an incident in other infections than by the meningococcus. "Cerebrospinal fever" connotes an acute specific disease, which is the idea we wish to convey by the name. "Meningococcus infection" would bring the various pathogenic possibilities of the micro-organism into line with those of the pneumococcus, with which it has close analogies. But just as "pneumonia" is a convenient term to express what is by far the commonest disease-process caused by the pneumococcus, so "cerebrospinal fever" is justified because it expresses the disease process most frequently caused by the meningococcus.

that the mucosa in these regions is the usual nidus of the microbe. The route by which the coccus reaches the meninges, whether directly through the bones at the base of the skull or through the blood-stream, is unknown. It is possible that a different route is taken in different cases.

Is there a Meningococcus Pharyngitis apart from Meningitis? —This is a very important question, but one that is extremely difficult to answer. The flora of the mucosa of the throat, when this is the seat of catarrh, usually yields a mixture of micro-organisms on examination; and it is not often easy to decide which is chiefly responsible for the inflammation. But very suggestive points are, (1) that the meningococcus is in some cases the dominant microbe grown; (2) that this is more consistently the case if the swab is taken directly from the pharyngeal wall, where the catarrh is often most marked; and (3) that these cases of acute or sub-acute pharyngitis yielding meningococci as the dominant micro-organism are more common in the epidemic areas. Such considerations have led some observers to hold the view that cerebrospinal fever has an initial catarrhal stage which may, or may not, pass on to a general infection, and, still later, to meningitis.[1] This is scarcely the place to discuss the matter at length. Reference may, however, be made to the fact that catarrhal conditions of one or other part of the upper respiratory tract are common at the outset of several specific fevers; that a "septicæmic" stage undoubtedly exists during the first few days of pneumonia, and during several days at the beginning of typhoid fever; so that this point of view in regard to cerebrospinal fever does but bring it into line with other acute infections. The question is bound up with that of nomenclature, to which reference has been made in the footnote on p. 636. However this question may be settled ultimately, it remains a fact of great significance that the more extended bacteriological investigations of recent years have demonstrated undoubtedly, that the meningococcus is present in a large number of throats examined during a period of epidemic. The practical importance of this fact can scarcely be exaggerated. The influence of *mixed infections* is doubtless

[1] *See* an important paper by Lundie, Thomas and Fleming in the *Brit. Med. Journ.* for March 20, 1915.

great; cerebrospinal fever epidemics occur during the winter and early spring, at which seasons catarrhs associated with the pneumococcus, M. catarrhalis, streptococci, and other less common micro-organisms are specially rife. A correspondence as regards incidence between cases of pneumonia and of cerebrospinal fever has definitely been established.

Incubation Period.—This appears to be variable, but it is probably short. Observations tend to place it at about four days.

SYMPTOMATOLOGY.

Clinical Types of Cases.—The disease is protean in its features, and especially in its modes of onset. This fact is daily being borne in upon the mind of the practitioner more and more, as he himself becomes faced with manifestations of it that defy his preconceived ideas and the knowledge he has got from text-books and teachers. It is not so much that his eyes are closed to the possibility of cases arising in his own practice as that he scarcely knows what to look for, and therefore fails to recognize the stigmata of the infection when they face him. No doubt the safest attitude, pending personal experience of the disease, is to be suspicious of all cases of acute illness which do not conform to well-known categories. *Quod non est præter naturam non fidendum.*

Out of the large number of different manifestations that occur, certain cases repeat themselves with sufficient constancy to constitute "types" capable of description.

I.—THE ORDINARY TYPE.

This begins with the symptoms of an acute specific fever, and for the first day or two there may be nothing to distinguish the illness from one or other of several acute febrile infections. The *onset* is usually sudden, with headache, fever, general malaise, and, very often, vomiting. The *headache* is apt to be very intense, is often localized at the occiput, and shows little or no response to the customary palliative drugs given to relieve it. The *temperature* usually rises rapidly, and attains a fairly high degree early in the onset (103°–104°). There is frequently a *rigor* in the adult, or a *convulsion* in the infant or child. *Vomiting* is more often met with in children than in infants, and is quite common in young

adults.

In addition to the three cardinal symptoms at the onset, headache, fever, and vomiting, the following are quite common, but are not nearly so constant:—*delirium, pains in the neck and limbs*, and some degree of *catarrh* either of the nose, nasopharynx, conjunctiva, or ear. In some cases there may be considerable bronchial catarrh, and in others definite enteritis. In addition to the pains referred to the limbs, there may be actual *swelling of joints*. After from 24 to 48 hours of these initial symptoms, evidence of meningeal irritation begins to show itself:—

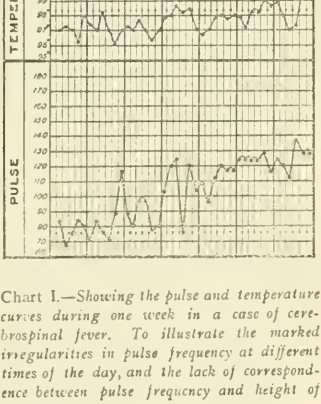

Chart I.—*Showing the pulse and temperature curves during one week in a case of cerebrospinal fever. To illustrate the marked irregularities in pulse frequency at different times of the day, and the lack of correspondence between pulse frequency and height of fever.*

1. *The Pulse*, though frequent, often shows a relative infrequency as compared with the temperature. This relative infrequency, however, may not be noticeable if the case is a very severe one. The frequency may then be relatively greater than the height of the temperature. The frequency is apt to vary much from hour to hour, and from day to day, even when the minimum frequency is high. This feature, and the general lack of correspondence between pulse frequency and height of temperature, is illustrated in Charts I.-III. The pulse rhythm is often affected, causing irregularity.

2. *The Respirations* are frequent, and, like the pulse, are apt to show irregularity in rhythm—either the Cheyne-Stokes type of breathing, or, as is more usual in older children and adults, a less periodic type, showing long intervals of apnœa or deep sighs.

3. *Facies and Posture.*—The vasomotor control is lost very

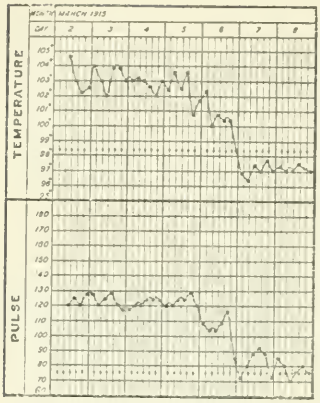

Chart II.—*Showing the pulse and temperature curves during one week in a case of pneumonia. To illustrate the relative uniformity of pulse frequency and the correspondence between pulse frequency and height of fever.*

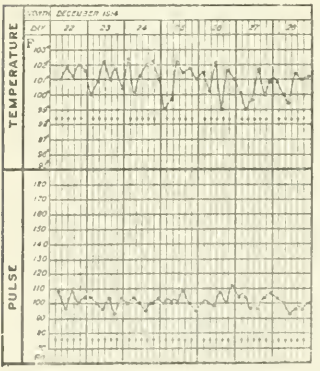

Chart III.—*Showing the pulse and temperature curves during one week in a case of typhoid fever. To illustrate the relative uniformity of pulse frequency and the correspondence between pulse frequency and height of fever.*

early; indeed, it is perhaps the first sign of direct nerve involvement. The face is flushed, but this flushing of the face is apt to vary from hour to hour. Quite early it may be noted that the patient chooses to lie on his side, and is uncomfortable if placed on his back; such an observation may lead to examination of the neck muscles, which are then found to be a little stiff (*v. i.*). The legs are often kept bent at the knees.

4. *The Mental State.*—Delirium is very common though by no means invariable. Coma is not present until the condition of the patient is practically hopeless, either because the type of case is fulminating, or because the diagnosis has been long delayed and the intracranial pressure has become very high. Earlier than this it is generally possible to rouse the patient from his condition of stupor. Exacerbations of great restlessness, with complete insomnia, are common, and it may even be difficult to keep the patient in bed. These mental crises by no means

indicate a fatal issue, but they raise the question of a further drainage of the cerebrospinal fluid if this has already been done earlier in the course of the disease.

5. *The Reflexes and the Knee-jerk.*—No general rules seem to apply, and very little value must be attached to these in making a diagnosis. The knee-jerk is so often absent in severe cases of many acute general infections (*e.g* pneumonia), that its absence here gives no help. Perhaps its presence is actually a slight point in favour of cerebrospinal fever in a doubtful case. The extensor plantar response (Babinski's sign) is often present, but it must be remembered that, like Kernig's sign, it is physiologically present in infants.

6. *Sensory Disturbances.*—Pain is quite common at the onset of the disease, and may be referred to almost any part,—a whole extremity, or one or more joints. Hyperæsthesia is another common feature,—especially in the form of intolerance for light and noise.

7. *Eye Changes* :—

(*a*) *The pupils* show many variations. The most common change is dilatation, a condition which is said not infrequently to be increased by stimulation of the skin of the neck, or by attempting to overcome the stiffness of the neck muscles.

(*b*) *Squints* may be present, and *nystagmus* is not uncommon.

(*c*) *Optic Neuritis* is not usual, and is certainly later to appear in this disease than in tuberculous meningitis.

8. *Stiffness of the Neck.*—Too much importance cannot possibly be attributed to this sign, and *it should be searched for early rather than be allowed to attract attention after it has become a marked feature.* It is probably present in a slight but definitely ascertainable degree very early in the disease, and its discovery, in the absence of local causes, is of the utmost moment, for it determines at once the question of lumbar puncture. Reference has already been made to the fact that the patient declines the supine position, because this brings the occiput upon the pillow and thus puts the muscles of the neck upon

the stretch, whereas the lateral posture allows the occiput to fall back and flexes the affected muscles. But in all cases in which cerebrospinal fever is suspected, the neck must be examined carefully and critically by placing the occiput in the hollow of the hand and testing the movements of the head, especially that of dropping the chin forwards. It is of value to remember that a very slight and doubtful degree of rigidity present at the beginning of this examination may become much more definite and unmistakable after a few movements are undertaken. The examination, therefore, should not be hastily abandoned as negative, but very thoroughly persisted in until it is certain that no stiffness exists. It must be remembered, too, that at an early stage of the disease the stiffness of the neck may be transitory; the examination should, therefore, be repeated frequently. If the patient is an adult, and is fully conscious, his statement that the manipulations are uncomfortable is in itself a suspicious thing, even in the absence of definite rigidity.

As the meningeal inflammation increases, the rigidity becomes persistent and unmistakable, and spreads to the rest of the spine, which becomes poker-like; so that, in a child, the whole body can be raised from the bed in a fully extended position by the hand placed behind the occiput.

Two further results of this increased rigidity may be present: *retraction of the head* and *opisthotonos*, the whole spine being arched so that the occiput and the sacrum form the extreme points of a curve with its convexity forwards. These two features are much more common in infants than in older children or in adults; they are almost constant signs in the sporadic cases of cerebrospinal meningitis, originally designated "cervical opisthotonos of infants" (Gee and Barlow).

9. *Kernig's Sign.*—This sign is nearly, or quite, equal to neck rigidity in its importance as a diagnostic point. It is due to a slight stiffening of the hamstring muscles, resulting in the patient's inability to keep the knees extended if the hip is flexed. It may be sought for in two ways—

(*a*) By raising the shoulders from the bed, so that the body is bent at the hips; the legs will be drawn up into a position of flexion at the knees.

(*b*) By raising the fully-extended leg with the body lying

flat on the bed; as the hip becomes more and more flexed, the knee cannot be kept extended nearly as long as it can in health.

Kernig's sign is present as a physiological condition in infants up to the age of about two years; it is, therefore, without pathological significance until after this age.

To complete this account of the clinical picture, it remains to consider three other features in the symptom-complex, not entirely referable to the meningitis, but to the general toxic state as well.

1. *The Temperature.*—The temperature chart in cerebrospinal fever shows no very constant type. In almost all cases the temperature rises suddenly, and in the fulminating and hyper-acute cases to a considerable height. It usually remains high in the malignant type, the patient dying oftimes with a true hyperpyrexia. In the very acute cases, the chart often presents the picture of a continued fever, with but slight remissions, like that seen in typhoid during the second week. In less acute cases (the "ordinary" type), the form of the temperature varies very considerably. Quite often it can only be called an irregular fever of moderate degree, falling gradually to normal with the subsidence of the acute symptoms.

Sometimes the onset, if the temperature happens to be for some reason recorded from the very beginning, is seen to be marked by two or three days of quotidian intermittent fever, followed by a more continued but irregular type. This is illustrated in Chart IV., Plate XLI., from a case in which the cerebrospinal fever began abruptly on the fourth day after the termination of fever due to measles. This chart also illustrates very well the sharp fall in temperature following lumbar puncture and the use of serum, the fever ending by crisis after the second puncture.

Another type of chart shows a tendency for the fever to become quotidian intermittent after the first week or two, and remain so for a considerable time. Chart V., Plate XLI., illustrates this. In this patient the administration of quinine had the curious effect of deferring the rise of temperature for two or more days. There was no evidence of malarial infection, and the patient (a youth aged 17) had never been

out of England. Recovery was complete in this case. Some chronic cases show this quotidian fever for several weeks, or even months. On the other hand, some of the chronic cases are afebrile. In the "postbasic" type in infants absence of fever is quite common.

Occasionally sharp rises of temperature are seen, very frequently in cases that appear to be gradually mending, even when the original fever has subsided for several days. They may last a few hours only, or one, two, or three days. Tney are often accompanied by a return of the headache, by insomnia and restlessness, or by an increase of the stiffness. Sometimes no appreciable set-back occurs at the time of their appearance. (See § on course of the disease.)

2. *Skin Eruptions* are very variable, both in different epidemics and in different stages of the same epidemic.

(*a*) The small dark petechiæ, which gave the name "spotted fever" to the disease, are often quite absent. They are more common in fulminating and in very acute cases than in those that are less severe. These spots are apt to occur much more frequently in some epidemics than in others. They are rarely very extensive in distribution, often at most a few small hæmorrhagic spots about the abdomen, chest, and thighs. But occasionally they are very profuse indeed, and I have seen a child suffering from the disease, whose trunk was completely covered with minute purpuric spots like flea-bites.

(*b*) Quite as common, perhaps, as the purpuric eruption is the appearance, during the first three or four days, of rose spots scattered discretely over the body, and involving the forearms and legs as well as the trunk.

(*c*) A more equivocal rash, macular or scarlatiniform in character, may appear later in the course of the disease; this only raises difficulties in diagnosis from the acute exanthems if the day of their appearance in relation to the first day of the disease be not taken into account. These rashes are apt to be very evanescent, and they not infrequently synchronize with an exacerbation in the meningeal symptoms (*v. i.*).

(*d*) Herpes is very common, and is said by some observers

to be even more common in this disease than in pneumonia. It is not usually very extensive, but it may involve other areas than the customary one about the lips and nose, such as the inside of the mouth, the eyes, and the hands and feet.

3. *The Blood.*—The progressive anæmia present in all acute infections is present here as well. A marked leucocytosis occurs, and a common figure to find in cases of ordinary severity is 20,000–25,000. The meningococcus can often be isolated from the blood by culture during the first few days of the disease, showing that, in cases of the ordinary acute type, cerebrospinal fever is a general infection just as are pneumonia and typhoid fever. In the hyper-acute and fulminating forms positive blood cultures are almost constantly obtained.

Next in frequency to the ordinary acute type of case is

II.—THE HYPER-ACUTE TYPE.

It is not uncommon in young adults. The invasion symptoms are abrupt, and the patient is, from the first, very ill. Delirium is marked, with most tiresome insomnia, and the headache may drive the patient to a state of acute mania. The temperature is apt to be very high (104°–106°). The meningococcus is readily grown from the blood by culture, and may even be demonstrated in coverslip preparations made from the blood direct. After three or four days the active mental state changes to stupor, and, if the cerebral pressure is not relieved by lumbar puncture, this passes on to coma. Even then, there is a great tendency for the patient to slip back into a similar state, so that, with pulse and respirations rising in frequency, insensitive pupils and absence of corneal reflex, the vital functions rapidly fail and death occurs.

III.—THE FULMINATING OR MALIGNANT TYPE.

This form is more apt to occur during the evolution of an epidemic than at other times. But it is by no means unknown as a sporadic manifestation of the disease. The abrupt onset of fever, headache, and delirium, rapidly passing into coma, the whole course of the disease may not exceed twelve hours. It may even be less: ". . . he went out to his father to the reapers. And he said to his father, My head,

my head. . . . And when he had taken him and brought him to his mother, he sat on her knees till noon, and then died." It is the occurrence of these fulminating cases that accounts for much of the horror associated with the disease in the lay mind. The newspaper records of inquests held upon victims of cerebrospinal fever indicate the abruptness of most of these cases and their rapid course.

IV.—MILD TYPE.

These cases are said to be common during the decline of an epidemic. It is, at present, quite impossible to say with what frequency they occur, because unless they are subjected to the confirmatory procedure of lumbar puncture, the diagnosis must always remain in doubt. But in the presence of an epidemic, a patient presenting the symptom-complex of headache, malaise, pains in the back and limbs, slight fever, and stiffness of the neck, is probably suffering from a mild grade of meningococcus infection. As there is no possible guarantee that the case may not show some rather sudden exacerbation, it is advisable in all such cases to proceed to lumbar puncture.

V.—POST-BASIC MENINGITIS OF INFANTS.

This is the disease originally described by Gee and Barlow under the name "cervical opisthotonos of infants." Most authorities are now agreed that the micro-organism causing this condition is identical with the meningococcus. The condition constitutes a persisting series of sporadic cases of meningococcus infection, with certain features that are apparently determined by the age of the patient. The anterior fontanelle bulges, and this yields a valuable aid to diagnosis. Although usually abrupt in onset, many of the cases quickly become sub-acute, and a fair proportion of them become chronic. The patients waste very considerably, and develop a secondary hydrocephalus which is often fatal. Complete blindness occurs with some frequency, and other affections, either of special senses or of motor functions, are apt to remain if recovery occurs.

These are the five types of the disease which deserve recognition. But aberrant forms occur, difficult of recognition, and until the symptoms of meningitis evolve, or some chance

material obtained from the patient yields an unexpected growth of meningococci, a diagnosis is scarcely possible. Thus, the case may come under treatment as a septicæmia without meningeal symptoms; or as a bronchopneumonia in a child; or simulating rheumatic fever by synovitis and profuse acid sweats.

COURSE OF THE DISEASE.

This is, fortunately, interrupted in a growing percentage of cases by modern methods of treatment. No more striking event occurs in modern therapeutics than the rapid amelioration of the symptoms in a case of cerebrospinal fever following lumbar puncture, drainage of the accumulation of inflammatory exudate, and the intra-spinal use of anti-meningococcus serum. There are three modes of termination, as there are in most diseases.

1. *Recovery.*—This is gradual when it occurs, and is often interrupted by sudden recrudescences, throwing the patient back into a state which calls for renewed anxiety. Even when a marked remission has occurred in the main symptoms, the patient is by no means safe from these "crises," which form a striking feature of the disease. They may be due to actual extension of the infective process into some further area of the pia-arachnoid system, or to mechanical events connected with the condition of acute hydrocephalus that exists, or to both of these. (See § on temperature.) If recovery takes place, it is usually during the second or third week in the ordinary type of case. Convalescence is not often interrupted. It may be some weeks, however, before the throat is free from the meningococcus.

2. *Death.*—Fulminating cases are invariably fatal by coma in from one to three days. Very acute cases show a high degree of mortality during the first week. The ordinary type of case is not usually fatal except by—

3. *Becoming chronic.*—If the "crises" already referred to continue, the patient passes into a state of progressive emaciation, with chronic hydrocephalus. The wasting is sometimes extreme. The rigidity becomes very marked, and approaches, even in adults, to that degree termed cervical opisthotonos in infants. Feeding becomes difficult, and this adds to the

wasting due to trophic disturbances. Optic neuritis develops. The temperature may be normal, or may show occasional sharp rises, or there may be a regular quotidian intermittent fever. The patient may continue in this unsatisfactory state for several weeks, or even months, and yet may eventually recover, without any undesirable residual defects. But more often than this he gradually succumbs to the disease, or recovers to be left with mental defect, amaurosis, deafness or hemi- or di-plegia.

DIAGNOSIS.

I.—FROM OTHER DISEASES, NOT PRODUCING MENINGITIS.

Fulminating cases of cerebrospinal fever are usually fatal before a diagnosis has been made. No doubt it is a sound principle to perform lumbar puncture in every case of deep stupor, or of coma, when the cause is obscure. Certainly this should always be done if fever is present too. It is extremely unlikely, however, that even this procedure would save the patient's life in this type of the infection. Blood culture almost always yields a positive result in these cases, but the patient is usually dead before the meningococcus has shown itself on the culture media. In the hyper-acute cases, the diagnosis becomes a matter of much more vital importance, for the gain of a few hours in treatment may undoubtedly save life time after time. These cases are often mistaken for severe forms of "*influenza*," for *pneumonia* before the appearance of physical signs, or for one or other of the *acute exanthemata;* less often, if the pains in the limbs are severe, for *rheumatic fever*. The ordinary type of case is, again, most often confused with "influenza," and even when cerebral symptoms develop these are too frequently thought to be toxic rather than due to inflammation of the meninges. The practitioner will do well to bear in mind the following helpful points in making the distinction between meningitis and toxæmia in a febrile case with "head symptoms":—

1. If *Headache and Delirium* occur at the same moment, meningitis is probably present, and not merely toxæmia. Contrast typhoid fever (toxæmia), in which headache and delirium alternate, the patient being apparently free from pain when he is delirious, with

cerebrospinal fever (meningitis), in which the patient is *delirious about his headache*. This distinction is an old observation, originally attributed to Sir Wm. Jenner, and it is one of great value.

2. *Vomiting.*—If this occurs, not merely at the onset of the fever but on subsequent days also, it is suggestive of meningitis.
3. *The Pulse and Respirations.*—Irregularities in rhythm are in favour of meningitis, and so is a relatively low pulse rate provided typhoid fever can be eliminated.
4. *Stiffness of the Neck*, without signs of otitis or other local inflammation, even though it exists only in a slight degree, is strongly in favour of meningitis; if the stiffness increases, rather than decreases, with examination, the presumption is greater still.
5. *Kernig's Sign*, provided the patient is over two years of age, may be taken as of equal significance with rigidity of the neck.

If one or more of these features is present in a febrile case of doubtful nature, the practitioner is justified in proceeding forthwith to lumbar puncture, without which an absolute diagnosis of meningitis cannot be made, still less the nature of the meningitis if it be present. Moreover, to perform the puncture is of great therapeutic value to the patient, should the disease turn out to be the more serious alternative, whilst no harm is done if it should be the less serious. Indeed, in certain acute infections such as pneumonia, when a state of "*meningism*" is present, or toxic head symptoms closely resembling those of meningitis, a lumbar puncture usually relieves the condition, and may quite abolish it.

II.—FROM OTHER FORMS OF MENINGITIS.

The distinction between meningococcus meningitis and *pneumococcus* or *influenzal* meningitis on clinical grounds is too speculative to require discussion; it must be settled by lumbar puncture. *Streptococcus* meningitis usually complicates some "septic" focus about the skull, and most often middle ear disease. *Tuberculous* meningitis presents these points of contrast: it is less abrupt in onset; the temperature is rarely

high (except as an ante-mortem event); rigidity of the neck is transient and ill-marked, or is absent; optic neuritis appears much earlier; in adults, aphasia is a common and an early symptom; true (paralytic) squint is common; in children, the "peevish" condition during the first week is much more marked; and in all patients the depth of stupor after the 7th to 10th day is much greater. But even these things are suggestive merely. It suffices only to decide that meningitis is probably present; the results of lumbar puncture must be relied upon to settle the nature of the infection.

LUMBAR PUNCTURE.

However high a degree of probability the result of a general examination may yield that a patient is suffering from meningitis, confirmation of this diagnosis rests entirely upon the results of lumbar puncture. For two reasons it should not be deferred: it establishes the diagnosis in the great majority of cases; and it is the most valuable point in treatment in the event of a positive result. It is probable that even to-day, with cases of cerebrospinal fever occurring over very widespread areas in this country, the great majority of practitioners are unacquainted with this important method of clinical investigation. This lack of knowledge should be repaired as early as possible. It is not necessary to wait for an actual case of suspected meningitis in order to become *au fait* with the technique of the process, for it may easily be learnt by practice upon the cadaver in the post-mortem room. With the intention of assisting the practitioner to perform the operation without difficulty, even in the absence of preliminary practice, the following account of the steps in the process has been made as explicit as possible.

The Question of an Anæsthetic.—If the patient is an infant, it can easily be held in the position about to be described by the nurse or assistant. In the case of a child, who cannot be made to understand the necessity of offering no resistance, a general anæsthetic is advisable. In an adult free from delirium or stupor, a local anæsthetic (ethyl chloride spray or novocain injection) is useful. In a delirious adult a general anæsthetic is necessary to avoid the arching of the back when punctured, which makes the procedure very difficult.

Choice of Apparatus.—Special apparatus are unnecessary.

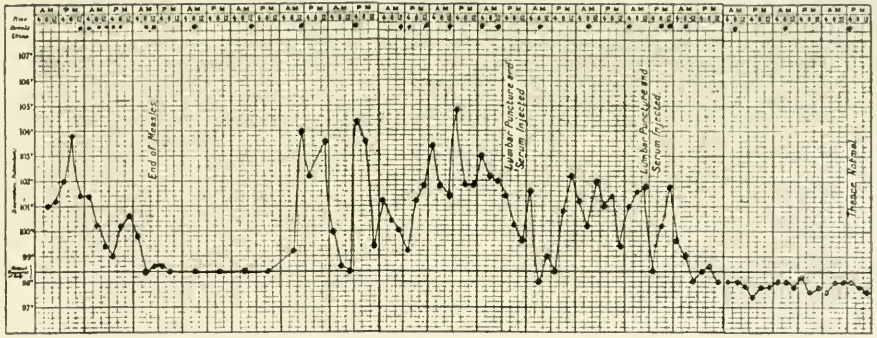

Chart IV.—*Showing onset of cerebrospinal fever on the fourth day after the fall of temperature due to measles. The onset is abrupt; the fever is intermittent for the first two days, thence onward it is continued and irregular, with marked remissions following lumbar puncture and the injection of serum.*

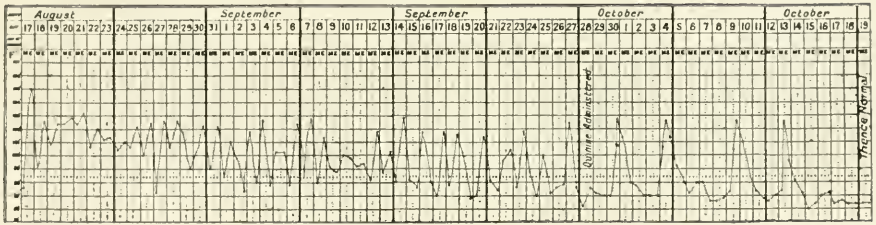

Chart V.—*Showing the quotidian intermittent type of fever after the first ten days.*

Fig. [illegible] showing position of patient and operator, and surface markings in the performance of lumbar puncture

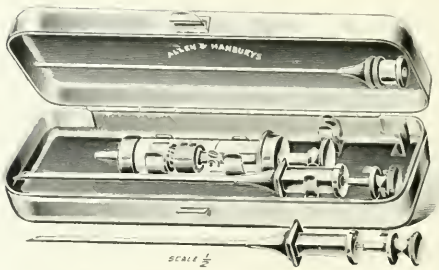

Fig. [illegible]—Barker's needle, used in lumbar puncture.

A long stout needle with a syringe may be used; but nothing is so useful as a "Barker's needle," which is strongly made and is fitted with a stylet the point of which is cut off flush with the point of the needle, whilst the other end terminates in a broad flat expansion to fit against the palm of the hand (Fig. 2, Plate XLII.).

Position of the Patient.—The patient is placed on his side near the edge of the bed and in a good light. The knees are drawn well up, and the head is bent forwards; the trunk is thus arched with its convexity backwards. Care is taken that the shoulder lying on the bed is not resting upon a pillow.

Surface Marking for the Puncture.—Draw a horizontal line between the summits of the iliac crests. The posterior spinous process lying nearest to this line is that of the fourth lumbar vertebra. The puncture is best made between this spinous process and that of the fifth lumbar vertebra, which will be felt from one-half to one-and-a-half inches below it, according to the age of the patient. The puncture is made in the middle line in an infant or child, and about one-third of an inch to either side of the middle line in an adult, so as to avoid the tense ligaments lying in the exact mesial position, which are difficult to pierce. The needle may be inserted directly in young patients, but in an adult it is useful to make a preliminary puncture of the thick skin by the point of a sharp scalpel (Plate XLII., Fig. 1).

Making the Puncture.—The region of skin which includes these two vertebræ is now thoroughly cleaned with soap and water, followed by acetone or alcohol; or it may be rubbed or painted over with iodine in spirit. Entering at the spot indicated the needle is directed forwards and, in an adult, with a slight inclination upwards and inwards. If obstruction be encountered, this is probably by bone; the needle is withdrawn a little way, and its direction is slightly altered in the vertical plane until it is felt to enter the canal. The distance the needle is inserted varies with the size of the patient,—from 1½ inches in an infant to 3½ inches in an adult. It is advisable to test the position of the needle as soon as it is thought from the "feel" that it has entered the theca. In this way the operator avoids piercing the venous plexus at the other side of the canal,—the common source of the blood that

occasionally flows, and which obscures the result of the puncture. If a "dry puncture" results, it is because either the needle has not entered the canal at all, or has struck a nerve-root, or the inflammatory exudate is too thick to flow through it. The first possibility is the most probable, the last very unlikely.

Collection and Examination of the Fluid.—Assuming a "Barker's needle" to be used, the first few drops of fluid are allowed to run into a vessel containing an antiseptic and are discarded. A sterile bottle or test tube is then placed to collect the remainder of the fluid, and is forwarded with due precautions to the pathologist. The amount of fluid allowed to flow will depend upon the pressure under which it exists and its relative turbidity. If the fluid spurts out, as though pent up, it may be allowed to flow until some 20 or 30 c.c. are collected. If it is turbid, again it may be allowed to flow for some minutes. In both instances a definite therapeutic value attaches to the removal of the fluid, quite apart from the injection of serum. If, however, there is no more pressure than normal (and this is greater than would be supposed by those unaccustomed to perform lumbar puncture), the needle should be removed when about 10 c.c. have been collected.

In health the cerebrospinal fluid is quite clear, limpid, and colourless. If it is even in the slightest degree opalescent, still more if it is definitely turbid, meningitis is present, and this may be confidently diagnosed without waiting for microscopic confirmation. The admixture of a few blood cells may give a spurious imitation of turbidity due to inflammatory products, but the condition may be recognized by noticing that the fluid thus affected is straw-coloured and has the appearance of silkiness due to the presence of red blood corpuscles suspended in a saline solution. If more than the merest trace of albumin is present after boiling the fluid and adding acetic acid, this is further evidence of meningitis. The rest of the examination, necessary to decide the nature of the meningitis, requires histological and bacteriological investigation.

FRAUDULENT AND NEURASTHENIC CASES.*

By SIR JOHN COLLIE, M.D., J.P.

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THE following notes are based upon one hundred consecutive cases of neurasthenia, during the last seven years, in patients whom I have been successful in inducing to submit to the modified Weir Mitchell treatment.

In diagnosing traumatic neurasthenia, a valuable asset is a knowledge of human nature as well as an experience of similar cases. Justly to estimate how far a patient's symptoms are attributable to his or her own faulty mental processes, one must have much more than a passing acquaintance with the symptoms of traumatic neurasthenia, hysteria, and malingering.

I purpose first to deal with the symptoms of neurasthenia, and then to mention a few of the special symptoms of the variety known as traumatic neurasthenia.

SYMPTOMS OF NEURASTHENIA.

Neurasthenia is essentially a mental state, but it often has some bodily disorder associated with and underlying it. It is primarily a bankrupt condition of the individual's nervous force, whereas hysteria is a disease of self-suggestion. The symptoms of neurasthenia are innumerable, but the following are some which I have met with most frequently.

There is often inability to make up the mind as to any particular course of action; most patients vacillate and cannot force themselves to do even what they really wish to do. If responsibility is forced on them, it produces mental confusion. Many complain of loss of memory; there is really no such loss, but merely an apprehensiveness produced by magnifying those trifling lapses of memory, which are so common with those past middle life. Symptoms which are almost invariably present are inability to fix the attention for any length of time, and incapacity for mental work. Most suffer from sleeplessness. All are obsessed with the idea that they will never be them-

* Paper read before the Medico-Legal Society.

selves again. Most of the unfortunate people suffering from this complaint live in a state of perpetual mental anxiety, stress, and morbid introspection, and seem to suffer from too great a permeability of their subconscious centres. The normal stimuli to consciousness seem either to be multiplied or to have become more acute. Such patients are nearly always irritable. Nine-tenths of the subjective symptoms met with in neurasthenics are the result of auto-suggestion.

A highly organized nervous system is a valuable equipment in life, but it has its disadvantages. It has been well said that neurotic people are the salt of life, but you can have too much even of that useful commodity. The personal equation and the mental outlook have much to do with how we perceive things. Working class people, whose intelligence and education are limited, have their mental perspective distorted, and often allow bad habits of thought to derange the adjustment of their normal mental equilibrium. When ill they seem voluntarily to surrender all will-power, and allow their thoughts to run unchecked along the lines of least resistance; in consequence, the whole mind is dominated by habitual self-observation and a self-induced loss of the sense of proportion.

Hyperæsthesia of various portions of the body is one of the most common features of neurasthenia. The hyper-sensitiveness, which prevents the turning of a deaf ear to such things as the increased beating of the heart, the sagging movements of the intestines, and the various sensations usually incidental to atonic dyspepsia, is always present. Sensations which normally constituted people ignore are also sources of pronounced mental anxiety, and neuralgias of all sorts are generally present, sometimes, in severe cases, accompanied by photophobia.

There is often complaint of headache of the type described as "a feeling of weight on the top of the head." The various reflexes, especially the knee jerks, are exaggerated, and the facial expression is always one of anxiety.

Neurasthenics always lose much weight. I have not been able to get a complete record of the weight in all these cases, but of the sixty-six cases in which the weight has been recorded, fifty-five gained weight: the gain varied from a few ounces to 12½ lbs., and the average was 4 lbs. 3 oz.

TRAUMATIC NEURASTHENIA.

One of the most thorny problems of medical jurisprudence

is to determine how much of a disclosed condition is the effect of trauma and shock, and how much is due to a faulty nervous system or a perverted mental outlook.

It should be understood that in traumatic neurasthenia many of the symptoms previously enumerated are present, but, looming largely, is the super-added fact that the individual has been the subject of an accident. This obsesses him; everything else is of no importance. The pain is *focussed upon* the seat of the alleged injury, and the fear that total incapacity will be the result of the happening of the accident takes possession of the patient. In severe cases, this is always so, and even in slight cases the memory of the accident seems to haunt the patient.

There is generally much tremor and mental depression. Neurasthenia, especially traumatic neurasthenia, is always a puzzle to a layman, who generally believes the subject of it to be a malingerer or a hopeless physical and mental wreck. We doctors know better, for we know of scores of cases which have been wholly cured, and the object of this paper is to demonstrate that a very much larger proportion, than has hitherto been thought possible, can be more or less speedily restored to health by appropriate treatment.

For instance, the condition so well-known twenty-five years ago as "Erichsen's railway spine," otherwise known as "concussion of the spine" (by which was meant concussion of the spinal cord) is *now known* as "hysterical spine"; it is merely a psychical condition, which is particularly intractable unless intelligently treated.

It is not generally appreciated that traumatic neurasthenia can occur without any actual traumatism. Many such instances have come under my observation.

For instance, I saw a case of undoubted traumatic neurasthenia produced in a young Jewess, who suddenly saw the head of a horse protrude through the plate glass window of a tramcar in which she was seated.

Recently, I had a woman under my care, who whilst at work heard a loud explosion in an adjoining building. She happened at the time to be in a poor state of health. Both her husband and father had died in consequence of accidents, and the mental effect of the shock produced symptoms, indistinguishable from those which would have occurred had she been actually physically injured.

I recall another instance. The driver of one of the motor fire engines of the London Fire Brigade knocked down a child when driving it. One of the wheels went over the child's head, and cerebral tissue protruded

from the fractured skull. The dead body was placed at the driver's feet, and he was instructed to drive to the nearest station. The man received no sort of injury, indeed, he was not even unseated, but he suffered from a pronounced attack of traumatic neurasthenia.

I saw, in a London hospital, a man who had been in an accident, but had admittedly received only a slight injury, not even being concussed. The mental effect of the scene, however, took such possession of him that, shortly afterwards, he developed a violent hiccough of a spasmodic nature. This ceased when he was asleep, but was present almost continuously during his waking hours, and continued for over a year.

It has now been held that cases of traumatic neurasthenia, brought about without actual physical injury, come within the meshes of the Workmen's Compensation Act.

The Court of Appeal recently decided a case in which a collier went to the assistance of a fellow workman who, having been badly damaged, was bleeding from the head, face, ears and eyes; he picked him up and carried him away, but the injured man died a few minutes later. The allegation made was that the plaintiff had received a nervous shock which incapacitated him from work, and that he, therefore, suffered from an accident which arose out of and in the course of his employment. The Court decided that the condition was, in fact, the result of an accident whilst at work. The Master of the Rolls held that the nervous shock produced a physiological injury, and was the result of an accident arising out of and in the course of his employment. He further stated that he saw no difference in principle between the condition of a patient who was suffering from ordinary shock as the result of traumatism, and the physiological effect produced on the miner in this case.

In conclusion, I may make a few observations on these cases, which are not to be gathered from the analyses I shall subsequently quote.

Of the traumatic neurasthenics there were nine in which there was a strong suspicion, perhaps more than a suspicion, of guile; nevertheless, at the time when they were sent to the hospital for treatment they were hopeless cases from the point of view of work. In every case my suspicions were justified. It is interesting to note that, taking these nine cases by themselves, the *average* duration of absence from work before entering the hospital was no less than 663 days, the average number of days' treatment in hospital was 64. Of these cases, *two* resumed work at once after leaving, with the help of a little persuasion; *three* resumed work after court proceedings; *three* after a sum in settlement; and one *after* receiving a pension! The average number of days of absence from work

prior to entering the hospital in these cases is somewhat striking, being close on two years, but this high average was due to the fact that two of the cases had been on the sick list for nearly five years, one for three years, and one for nearly two years. There is often a very marked contrast between the length of time the disability lasted prior to examination and report, and the comparatively short time in which they were restored to health after institutional treatment.

Taking the hundred *as a whole*, it will be seen that, although the average number of days' absence per case before entering the hospital amounted to 219, the average number of days' treatment in hospital was 49, and of the hundred cases no less than 72 were cured.

Many cases would be settled without arbitration proceedings, if litigants who, consciously or unconsciously, exaggerate symptoms for the sake of gain, were taught that a firm determination to turn a deaf ear to their perverted sensations really makes for happiness, and that self-control, self-respect, and a return to work when able, are of more service and more lasting value than many coins of the realm.

In addition to the hundred cases enumerated, I had nine cases originally diagnosed as neurasthenia, which turned out to be cases of true mental derangement. Neurasthenia is not in any sense the initial stage, or a phase, of insanity, but there can be no question that to diagnose between incipient insanity and well-marked neurasthenia is sometimes almost insuperably difficult. The nine cases were, after the facilities for close observation which residence in a hospital affords, found to be mentally unhinged and not suffering, as I thought, from neurasthenia. I think, however, I may be pardoned these errors.

I well remember a case which came under my care, when I was in general practice; it was that of a highly strung lady who called upon me almost every morning, and declared she was sure she was going out of her mind. I called in consultation a well-known neurologist, who was very emphatic, upon my raising the point, that she was not suicidal. A few weeks later, I had to withdraw from the case, for she and her friends declined to follow out my treatment. Not long after she cut her throat, from ear to ear, with an ordinary table knife.

TREATMENT OF NEURASTHENIA, TRAUMATIC AND NON-TRAUMATIC.

There is no doubt that a large number of these cases

are mixed up with conscious or unconscious exaggeration and sometimes with fraud, but, when a man is genuinely ill and also exaggerates, the correct, indeed the only humane, treatment, is first to deal with the underlying genuine complaint.

Neurotics who have had an accident are, as a rule, much more in need of treatment than their traumatism.

All traumatic neurasthenics have the threshold of their consciousness temporarily lowered. The essential thing is to place the patient in the best conditions to lift successfully the threshold of their consciousness above the level of the stimuli which cause them discomfort. As a rule, this only obtains in a new environment—away from sympathizing friends. When from home they are more easily made to realize that the facility with which their sensations worry them is, to an extent, self-induced, and they are gradually made to feel that it is their duty and to their profit to help those who are trying to lead them out of themselves.

Counter-suggestion, if it is to succeed, must be immediate, forcible, and continued, and must be applied at the psychological moment, for a traumatic neurosis depends not so much upon a physical injury as upon an exaggerated *idea* of the injury.

In hospital, automatically, and by comparatively little, if any, effort on their part, their self-interest and self-pity are relegated to the background, by reason of their attention being attracted by the novelty of fresh surroundings. That this is so is demonstrated by an immediate diminution in the complaints made. Patients in hospital are subjected to the *massive* suggestion, afforded by the hospital atmosphere, and the environment of discipline, the results being most satisfactory.

Next in importance to the removal from their home circumstances is the influence of an independent, experienced, and judicious nurse, and, lastly, a doctor who is sure of his diagnosis, confident of success from previous experience, and possessed of a strong personality.

Until the importance of early and proper treatment is recognized, and its provision enforced, the ever-increasing burden imposed by compensation to workmen will not be really checked or reduced.

Isolation and residence in hospital of itself does not necessarily produce a complete cure; occasionally, a few weeks at

a convalescent home are required to complete the recovery.

One important point with regard to institutional treatment of neurasthenia is that, where possible, the patient should contribute some portion at least of the cost of maintaining him in the institution. This should enlist his active co-operation in the cure.

Neurasthenia is a disease which usually proves very expensive to everyone, and I am confident that, even if the employer or the insurance company has to defray the hospital charges it is a good investment.

In non-traumatic cases, I have, in some instances, arranged that on return to work half-time should be allowed for the first week, and the amount of work each day gradually increased subsequently until full work is accomplished. Unfortunately, in traumatic cases this is not practicable for very obvious reasons, connected not only with the labour market but with the mental attitude of the injured person.

My experience is, that to send convalescent traumatic neurasthenics to a working man's convalescent home is a mistake. Although the furnishing of these places is very good, the accommodation clean, and the food wholesome, yet the whole environment is dull and dispiriting. The total absence of any attempt to provide wholesome occupation has a prejudicial effect upon those who are of the introspective type.

In the best sanatoria, patients convalescing from tuberculous disease of the lungs are, for many months before leaving, expected to engage in hard, laborious work. The late superintendent of Frimley Sanatorium used to show with pride a large reservoir which his convalescent patients had dug for the institution. Too often, a convalescent home reminds one of the epileptic or demented wards of a lunatic asylum. Sitting accommodation strikes one as obtruding itself everywhere, chairs are found arranged in groups, but nothing in the way of healthy, useful, purposeful occupation, such as carpentering, gardening, etc., seems to be thought of. Enforced idleness, combined with segregation, obviously opens the door to that interchange of medical experience so detrimental to the advance of the convalescent stage in all diseases, especially neurasthenia.

I find success is more likely to be assured by sending a patient straight to work, after the interval of but a few days.

In the institution where most of my cases of this character are treated, proper physical exercises and the gradual hardening process form part of the treatment.

EFFECTS OF EXPECTATION OF PENSION.

Many of the people I have to deal with are entitled to a good pension for life, if permanently incapacitated. Some with whom I had wrestled for months, even for years, eventually obtained their pension, and after receiving it returned to other work within a few months!

Such people are very difficult to deal with. Too often crafty workmen encourage an illness, so that they may obtain their pension, and, because the imposition cannot be proved, one sometimes has actually to recommend a pension, well knowing that what really amounts to a fraud is being perpetrated.

The following case illustrates what I mean:—

P. P. P., a seaman, aged 25, sustained bruises of the head and back under circumstances which entailed much notoriety and many newspaper paragraphs. He did not sustain any really serious injury, but, when sent to me two months after the accident, he kept his back bent at an acute angle, declaring he could not take off his clothes, but eventually did so, and put them on with some alacrity. His woe-begone appearance, and his apparent helplessness during my examination were in strong contrast to his subsequent behaviour, for he was observed outside my house laughing and gossiping with strangers.

As is so usual in these cases, his medical attendant diagnosed an obscure spinal lesion. He was obviously fit for work, and as I reported to that effect, he resumed forthwith.

After forty-one days he again put himself on the sick list, and his medical attendant reported that his pluck and nerve were gone beyond all recall. He obviously did not intend to resume his usual work again, so I obtained his admission into hospital where it was noted that his appetite was good, that he slept well, that he was mentally clear, that all his reflexes were normal, but that he had an hysterical loss of sensation. He remained in the hospital for thirty-three days, and was then sent for three weeks to a convalescent home, after which he was ordered to return to work. This he did, for one month only.

He was now said to be unable to stoop or kneel on account of pain, and his medical attendant became more convinced that he had an "organic lesion" of the spinal column. He was accordingly again sent to me for examination and report. It was obvious that he had no desire to get well, that he was hysterical, and was suffering markedly from pensionitis. He was a self-made neurasthenic for medico-legal purposes, but I hoped prolonged hospital treatment would lead him out of his morbid mentality, therefore I arranged for his admission into another nerve hospital.

He remained there for four months. The house surgeon reported that

he still had "pain and tenderness in the back" (presumably he *said* he had pain and tenderness in the back), that at first he improved "to a slight extent but latterly very little." No organic disease of any sort had been discovered.

On leaving the hospital he still held his back at an obtuse angle, and when asked to touch his toes his attempt was a pantomime display. He was then sent to a convalescent home for four weeks. On his return from the convalescent home, he was seen by his medical attendant, who now attempted a more exact diagnosis and suggested Locomotor Ataxia as being approximately correct. It was thirteen months since his accident, and I was called upon to report definitely as to his fitness or otherwise for work, a decision which is always sooner or later forced upon me. I certified him as permanently unfit for further service, and stated the cause as Traumatic Neurasthenia, but I was well assured that he really was a Malingerer. I certified thus, because I knew I could not substantiate a charge of malingering. In reporting him unfit I detailed the circumstances, and ventured to predict that, after receiving his pension (which must follow my report), he would be at work within six months. Curiously, it turned out that was the exact period at which he did in fact return to work, with, of course, his pension of twenty-five shillings a week for life!

It may be urged that many of these people should not have been pensioned, but in some cases, for instance that of a fireman, a man may be of no real practical use in the rough and tumble and serious duty in the London Fire Brigade, even though he might be well enough to parade in gorgeous uniform in front of the house at a theatre. Moreover, no man who dislikes his work so much, that he wants to leave it, can be really efficient.

SYNOPSIS OF A HUNDRED CONSECUTIVE CASES OF NEURASTHENIA.

——	Total.	Cured.	Improved.	Failure.	Discharged Self.	Average Number of Days absent from Work before entering Hospital.	Average Number of Days treated in Hospital.
I. Neurasthenia, traumatic.	32	17	4	8	3	465	61
II. Neurasthenia, non-traumatic.	57	49	3	4	1	39	40
III. Malingering (all accident cases except one).	11	6	—	5	—	434	60
Totals -	100	72	7	17	4	219	49

SECTION 1.—TRAUMATIC NEURASTHENIA.

Number.	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History
1	Public body	Fireman	Accident, traumatic neurasthenia and hysteria.	93 days	41 days	Failure (but pensionable).	On leaving hospital improvement not kept up. Five months after leaving certified permanently unfit. Retiring pension 30s. a week. On inquiry three years later it was ascertained he had done no work since retirement.
2	Public body	Driver	(1) Accident to back, alleged "railway spine."	164 days	54 days	Much improved.	Six weeks after leaving hospital resumed light duty for three months, then relapsed.
			(2) On relapse complained of pain in head and insomnia. I was asked if he were likely to be permanently incapacitated and advised further hospital treatment first.	—	73 days	Cured	Sent convalescent home and resumed work five weeks after leaving hospital. Since his return to work has been engaged on clerical duties, satisfactorily performed; no indulgences being asked or granted. Five and a half years after appeared in fairly good health.
3	Public body	Conductor of public vehicle.	Alleged electric shock. Neurasthenia.	23 days	42 days	Cured	Went country and resumed two weeks after leaving hospital.
4	Insurance Company.	Van driver	Injury to back. Typical traumatic neurasthenic. Had let himself go.	434 days	45 days	Cured	Resumed his old work immediately on leaving hospital. £89 paid in compensation, medical charges and hospital fees.

5	Solicitor for Shipping Company.	Captain of sailing vessel.	Fall, injured back, pronounced hysteria.	302 days	51 days	Cured	On leaving hospital reported fit for duty and did it.
6	Insurance Company.	Painter	Accident, traumatic neurasthenia.	103 days	3 days	Discharged himself.	Settled for £30.
7	Public body	Fireman	(1) Traumatic neurasthenia (2) Two years later had a relapse into neurasthenia.	30 days 48 days	58 days 28 days	Relieved Failure	Resumed work. Permanently unfit, further service. Pension 25s. a week. Shortly after obtained work as yachtsman.
8	Public body	Labourer, employed at light work.	Fractured thigh, long since recovered, but would *not* work. Functional neurosis.	124 days	29 days	Cured	To begin light work.
9	Public body	Fireman	Traumatic neurasthenia after injury to head ten months before, after which he had resumed work until present occasion. Hopeless neurasthenic, pension decided on, but sent to hospital with view to improvement prior to dismissal.	13 days	38 days	Failure	On leaving, sent to convalescent home for two weeks. Decided improvement. Pensioned as arranged on account of old-standing neurasthenia precipitated by accident. Received pension 25s. a week, and as there seemed little prospect of his ever being fit for work, he was considered entitled to £1 a week in addition under the Workmen's Compensation Act.
10	Shipping Company.	Labourer, aged 60.	Alleged pain in back and arm due to fall off quay, 10 feet. No spinal disease, but free movement. Comfortable income and sympathetic environment.	6 years and few days.	61 days	Cured	Mental attitude much improved; on leaving, it was arranged he should do light work at first, though *nominally* at full work. When informed by the Company, in accordance with my report, that he had wholly recovered he returned to work and gave no more trouble.

SECTION I.—TRAUMATIC NEURASTHENIA—*continued.*

Number.	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital	Results of Hospital Treatment.	Subsequent History.
11	Public body	Female office cleaner.	Traumatic neurasthenia. Unusual case, due to hearing an explosion. Husband and father had died of accidents.	86 days	40 days	Cured	Went to convalescent home, and resumed work three weeks after leaving hospital.
12	Shipping Company.	Labourer	Fall into ship's hold. Traumatic neurasthenia with pronounced functional symptoms. Poor physique. Poverty. Mentally dull.	1 year and 29 days.	51 days	Deliberately and intentionally procured dismissal by flagrant breach of discipline.	After he left hospital case settled for £40. He returned to work after spending it.
13	Shipping Company.	Ship scraper, aged 48.	(1) Fall 30 ft. Pronounced traumatic neurasthenia. Employer sent message to his own doctor to say he was to enter hospital; by mistake messenger reported he was to go to *Bethlem*. The doctor replied, "Quite right, I always thought he ought to go there!"	5 years and 8 months.	106 days	Improved	Much improved in hospital and sent back to work, but unsuitable work was provided for him at busy quayside beneath crane unloading ship.

			(2) Relapsed. Taken into hospital again.	—	127 days	Failure	Never regained the improvement he had made. Settled for £300. Enquiry nine months later showed he was living on compensation and was unable to resume work.
14	Insurance Company.	Married woman. Cook, aged 45.	Accident to arm. A neurosis.	155 days	10 days	Discharged self.	On leaving hospital she did not resume work, and 13½ months later case came before County Court judge, who made award in favour of employers.
15	Insurance Company.	Artizan	Fall on back. Neurasthenic.	339 days	60 days	Failure	Relapsed on return to sympathetic environment. Settled out of Court for £95 and £20 solicitor's costs.
16	Public body	Coachman	Knocked down and killed child but received no personal injury. Became obsessed with details of accident, pronounced traumatic neurasthenia. No improvement after few weeks in country.	50 days	31 days	Cured	Certified fit for duty on leaving, relapsed, became nervous when driving. Suspecting hysteria I advised he should continue driving but in less responsible capacity. This could not be arranged, and he was handed over to his superior officer, who effected a rapid cure by causing him to drive (under supervision) some 50 miles a day for 10 days through crowded streets.
17	Public body	Driver of electric tramcar.	Traumatic neurasthenia. Electric shock.	315 days.	125 days.	Improved	On leaving hospital resumed work. Two and a half years later still doing an ordinary day's work, but unable to drive vehicles again.

SECTION I.—TRAUMATIC NEURASTHENIA—*continued.*

Number	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History.
18	Public body	Clerical assistant.	Having been absent from work 23 weeks in a period of 9 months he was sent to me. It appeared that he had been told he was suffering from diabetes, because his urine gave a positive reaction with Fehling's solution on one occasion, the mental effect being a severe attack of neurasthenia.	163 days.	58 days	Cured	On leaving hospital he went to the country, and resumed work three weeks later. Four and a quarter years later, at the outbreak of war in August 1914, he volunteered and was accepted for military service.
19	Public body	Driver of electric car.	Traumatic neurasthenia after contusion of shoulder.	7 days	30 days	Improved	Resumed 23 days after leaving hospital. This man was seen six days after the accident; immediate treatment in hospital cut short what undoubtedly was shaping for a severe attack of traumatic neurasthenia.
20	Public body	Conductor of tramcar.	(1) Traumatic neurasthenia after injury to head and arm, exceptional case occurring 6 months after accident.	190 days	57 days	Improved	Went to convalescent home, and resumed work seven weeks after leaving hospital.

			(2) After being at work four months went sick again with functional hemiplegia; re-entered hospital.	—	43 days	Cured	Left hospital, and went to convalescent home for four weeks. Resumed work seven weeks after leaving hospital.
21	Shipping Company.	Ship's fireman and trimmer.	Fall down bunker, injured neck, chest, arm. Traumatic neurasthenia. Alcoholic.	367 days	49 days	Cured	On leaving hospital, employer provided light work. He gave it up, re-examined three months later, still traces of neurasthenia. Advised work of more congenial nature. Claim settled finally for £50.
22	Insurance Company.	Carman, aged 59.	Had an obsession that having had an accident, he was ill, alleged pain in back and side, that he was wasting away, and that even to attempt work was an impossibility.	4½ months	43 days	Cured	Compensation continued up to time of leaving hospital. On leaving resumed work at once.
23	Public body	Tramcar driver.	Two and a half years before had hernia, caused on duty. Operation for radical cure. Never wholly recovered from shock of operation. Frequent short absences from work with neurasthenic symptoms.	14 days	36 days	Failure	Resumed duty as motor man four days after leaving hospital. Again absent soon after, and it was arranged he should do work of less responsible nature.
24	Public body	Gymnasium attendant.	Accident. Traumatic neurasthenia and hysteria.	116 days	33 days	Failure (but pensionable).	Seven months after leaving, certified permanently unfit. Retiring pension of 25s. a week. Six months' later started work as fireman at a museum.

SECTION I.—TRAUMATIC NEURASTHENIA—*continued.*

Number.	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History.
25	Solicitor of public body.	Clerk	Street accident. Neurasthenia. Never were any objective signs of injury.	70 days	27 days	Failure	Cured when left hospital; admitted it; said "All I want now is work"; failed to obtain it; became hysterical. Then his neurasthenia relapsed. At arbitration proceedings four months after leaving hospital received between £400 and £500 compensation, soon after which he returned to work.
26	Insurance Company.	Labourer, aged 26.	Alleged sprained back lifting kerb stone. Seen by a doctor who advised he was malingering, but would become neurasthenic if not firmly dealt with. Allowed to drift. When seen by me 8¼ months after accident he was, in fact, a typical neurasthenic, obsessed with idea of injury.	261 days	58 days	Cured	On leaving hospital was sent to convalescent home for two weeks, at end of which period he was reported wholly recovered and fit for work. Again postponed return to work, sick allowance stopped, returned to work, and worked satisfactorily.
27	Insurance Company.	Baker	Fall down steps; valetudinarian.	4 years and 11½ months.	125 days	Cured	Recovered ultimately, but would not admit it. Employer nervous of fighting, offered small sum which he accepted. Had been receiving compensation for five years. Resumed work.

28	Solicitor of public body.	Domestic servant.	Complete hysterical paraplegia in neurotic subject after tramcar accident.	30 days	58 days	Cured	Rapidly improved, healthy influence of hospital made her take pride in recovering, walked within few weeks, went to convalescent home for three weeks, last fortnight there helped in waiting at table. Doctor at convalescent home reported wholly recovered. Returned home; two days later when seen manner wholly changed, complained of incapacity for work and pain in legs, but was out walking when called on. Mother and doctor interviewed, girl promised to return to work next morning and did so.
29	Insurance Company.	Tailoress	Dogbite. Hysteria.	189 days	43 days	Cured	Reported as fit for duty. Returned home. Dressed an absolutely healed wound with elaborate surgical dressings. Obtained sympathy and co-operation in her hysterical attitude. Advised fit for duty as from date on which she left hospital. Eight months later, at county court action, judge decided she was well as from the date of leaving hospital.
30	Shipping Company.	Labourer	Blow on head, traumatic neurasthenia.	4 years and $7\frac{1}{2}$ months.	87 days	Cured	On discharge certified fit to resume work, but declined until he was paid a sum in settlement, and then went abroad. Eight months later, wife (whom he left in this country) stated as far as she knew his head had not troubled him since.

SECTION I.—TRAUMATIC NEURASTHENIA—*continued.*

Number.	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History.
31	Shipping Company.	Ship's steward.	Fall down ladder. In bed a helpless invalid for three years and two months with complete paraplegia and paralysis of whole of left arm. Claimed £600 in settlement.	3 years and 2 months.	63 days	Improved	On leaving hospital could walk easily, sent to convalescent home for three weeks. He was then offered £50 in full settlement, which he agreed to accept with much alacrity. Agreement between owners and claimant recorded, finally disposing of liability. Regarded as satisfactory result.
32	Shipping Company.	Motorman	Marked symptoms of spastic paraplegia, believed to be functional.	1 year and 10 months.	82 days	Improved	Paralysis found to be functional. Alleged total incapacity. Nine months after leaving hospital at County Court action the weekly allowance was reduced from 20s. to 12s. as from the date he left the hospital. He made overtures to commute the weekly allowance for £50 five months after the arbitration, saying that he had secured an appointment abroad.
			SECTION II.—NEURASTHENIA, NON-TRAUMATIC.				
1	Public body	Stoker	Neurasthenia and over-strain of heart.	38 days	28 days	Cured	Fortnight after leaving hospital resumed outdoor work provided for him, as in my opinion he was genuinely unfit to act as stoker in future.

2	Public body	Clerk	Neurasthenia.	21 days	70 days	Cured	On leaving hospital went to convalescent home for six weeks, and then resumed. Never to do overtime, as no reserve strength, and unable to do overtime a normal man could do.
3	Public body	Clerk	Neurasthenia. Ill (though not absent) for a year previously from this cause.	4 days	42 days	Cured	Resumed work.
4	Public body	Clerk	Neurasthenia and alcohol. Wanted to go a sea voyage, but on my advice entered hospital instead.	56 days	26 days	Cured	Resumed work four days' after leaving hospital. Seen unofficially on several occasions since, and 1¾ years after illness still remaining fit and a total abstainer.
5	Public body	Clerical assistant.	Neurasthenia; had been ill some time previously, though not absent.	29 days	45 days	Cured	Went to country on leaving, and resumed seven weeks later. Never to do overtime again.
6	Public body	Plough repairer.	Neurasthenia, genuine; had frequent absences previously.	7 days	47 days	Cured	Went to convalescent home, and resumed 19 days after leaving hospital.
7	Public body	Stores foreman.	Neurasthenia and mental depression.	25 days	33 days	Cured	Resumed work 18 days after leaving hospital.
8	Public body	Fireman	Neurasthenia.	58 days	45 days	Failure	Permanently unfit for service. Received gratuity of £60. Subsequently employed as fireman at jam factory.
9	Public body	Warehouseman.	Neurasthenia.	27 days	51 days	Cured	On leaving went to convalescent home for three weeks and then resumed work.
10	Public body	Inspector	Neurasthenia.	64 days	23 days	Cured	Resumed outdoor work six days after leaving hospital.
11	Public body	Clerk of Works.	Neurasthenia.	44 days	41 days	Cured	Went to seaside. Resumed work two and a half months after leaving hospital.

SECTION II.—NEURASTHENIA, NON-TRAUMATIC—*continued.*

Number.	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital	Results of Hospital Treatment.	Subsequent History.
12	Public body	Fireman	Neurasthenia.	37 days	45 days	Cured	Resumed work three weeks after leaving hospital.
13	Public body	Solicitor	Neurasthenia.	About 7 days.	15 days	Cured	Resumed work a month after leaving hospital.
14	Public body	Clerk	Neurasthenia.	7 days	3 days	Discharged self after three days.	Resumed work four weeks after leaving hospital. Two years later he was said to be occasionally neurasthenic and excitable as if on verge of breakdown.
15	Public body	Engineer	Neurasthenia.	11 days	40 days	Cured	Resumed work four weeks after leaving hospital.
16	Public body	Correspondence clerk.	Neurastheuia, vertigo.	10 days	17 days	Cured	On leaving went to country and resumed 25 days later. Two years later he was still in same employ, having during that period been absent from work one week, giving neurasthenia as the cause.
17	Public body	Conductor of public vehicle.	Neurasthenia. Collapsed on duty, certified syncope, found much under weight and debilitated.	29 days	34 days	Improved	On leaving not wholly recovered. Given employment as pointsman. Two-and-a-half years later still continuing this duty satisfactorily.
18	Public body	Greaser and cleaner.	Neurasthenia.	120 days	43 days	Cured	On leaving hospital was given a week's leave before resuming work.

19	Public body	Surveyor's assistant.	Neurasthenia.	16 days	39 days	Cured	Resumed work two weeks after leaving hospital. Advised firm treatment.
20	Public body	Foreman	Neurasthenia. It was proposed to promote him to a more responsible position, but owing to certain nervous symptoms he was first submitted for medical examination, when short residence in hospital was advised.	5 days	36 days	Cured	He resumed his old work, but it was considered his health would remain at a higher level if he were *not* promoted to the more responsible position that had been designed for him.
21	Public body	Enquiry officer.	Neurasthenia.	82 days	32 days	Improved	Resumed work three weeks after leaving hospital.
22	Public body	Fitter	Functional nerve disease, alleged paralysis following attack of influenza.	49 days	53 days	Cured	Resumed duty at once.
23	Public body	Enquiry officer.	Neurasthenia.	11 days	30 days	Cured	On leaving hospital went to convalescent home, followed by annual leave. Resumed 41 days after leaving hospital.
24	Public body	Motor instructor.	Neurasthenia.	10 days	33 days	Cured	Sent to convalescent home for three weeks and then resumed work.
25	Public body	Enquiry officer.	Neurasthenia.	99 days	42 days	Cured	Went to seaside for two weeks and then resumed work.
26	Public body	Trenchman	Neurasthenia following influenza.	33 days	24 days	Cured	Resumed work week after leaving hospital.
27	Public body	Clerk	Neurasthenia.	58 days	27 days	Cured	Anxious to resume and allowed to do so 14 weeks after leaving hospital. Part time duty, arranged he should begin work three afternoons a week, then five, then all day. Seen six weeks after return to work, reached his highest level, a somewhat poor one.

Number.	Employer.	Occupation.	Details of Illness.	No of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History.
28	Public body	Clerk	Neurasthenia and mental depression.	12 days	34 days	Cured	Reported fit for work five weeks after leaving hospital.
29	Public body	Street foreman.	Functional paraplegia.	35 days	38 days	Cured	Reported fit for duty three weeks after leaving hospital. Delayed return, but ultimately resumed work two weeks later.
30	Public body	Clerical assistant.	Neurasthenia.	11 days	76 days	Cured	Improved slowly. Mental standard not high. Went country three weeks before resuming.
31	Public body	Collector of taxes.	Neurasthenia.	31 days	38 days	Cured	Resumed work two weeks after leaving hospital.
32	Public body	Fireman	Neurasthenia not due to service. Bad prognosis, recovery doubtful, but decided to try hospital.	28 days	51 days	Symptoms improved but failure.	Did not resume. Certified permanently unfit on leaving hospital. Vision too defective for his occupation. Shortly after retirement started light work as fireman at a theatre.
33	Public body	Park keeper	Functional paresis of lower limbs	48 days	37 days	Cured	Resumed duty five days after leaving hospital.
34	Public body	Artizan	Neurasthenia, advised hospital treatment but declined, went to country, finally entered hospital. Alcohol and tobacco poisoning.	48 days	30 days	Cured	Resumed two and a half weeks after leaving hospital.

35	Public body	Fireman	Neurasthenia after quarrel with superior officer. Question whether mental. After leave of absence hospital treatment advised for neurasthenia.	73 days	52 days	Failure	Never resumed. Five weeks after leaving certified permanently unfit on account of neurasthenia and defective vision. Gratuity of £92 19s.
36	Public body	Collector of licence duties.	Neurasthenia and mental depression.	28 days	42 days	Cured	Gained weight. Resumed work one week after leaving hospital.
37	Public body	Labourer	Alleged cardiac weakness. Introspective.	34 days	24 days	Cured	On leaving hospital returned to work. Began to absent himself again from work and was told that he must either work or go, and preferred working. Nothing heard of him since.
38	Public body	Turncock	Neurasthenia.	36 days	41 days	Cured	Went to country and resumed work 33 days after leaving hospital.
39	Public body	Clerk	Neurasthenia.	47 days	48 days	Failure	On leaving hospital went to country; 48 days after leaving reported permanently unfit, still neurasthenic, unlikely to be fit for continuous work, and wished to retire on account of his health.
40	Public body	Collector of taxes.	Severe neurasthenia brought on by overwork and worry.	23 days	36 days	Cured	On leaving went to seaside and resumed work 30 days later. Work to be permanently lightened.
41	Public body	Clerical assistant.	Neurasthenia.	59 days	36 days	Cured	On leaving went to country. Seventy-four days after leaving hospital resumed work. Arranged should do part time work first three weeks.
42	Public body	Clerk	Neurasthenia.	8 days	49 days	Cured	On leaving went to convalescent home for three weeks.

SECTION II.—NEURASTHENIA, NON-TRAUMATIC—*continued.*

Number.	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History.
43	Public body	Female clerk.	Neurasthenia and mental depression.	159 days	100 days	Cured	On leaving hospital went to doctor's family in the country and resumed work a month later.
44	Public body	Female ticket checker.	Neurasthenia.	27 days	73 days	Cured	Resumed work 25 days after leaving hospital.
45	Public body	Charwoman	Neurasthenia and mental depression.	79 days	39 days	Cured	Resumed work a week after leaving hospital.
46	Public body	Female typist.	Neurasthenia.	13 days	51 days	Improved	Arrangements made for her to go to convalescent home on leaving hospital, but meantime she resigned her position.
47	Public body	Female ticket checker.	Neurasthenia.	10 days	45 days	Cured	Went to country for two weeks and then resumed work.
48	Public body	Female ticket checker.	Neurasthenia. Went to country for four weeks before entering hospital.	41 days	59 days	Cured	Resumed work two weeks after leaving hospital.
49	Public body	Female typist.	Neurasthenia.	29 days	21 days	Cured	Resumed work two weeks after leaving hospital.
50	Public body	Female typist.	Neurasthenia.	34 days	43 days	Cured	Went to convalescent home for two weeks and then resumed work. Advised less strenuous work. After nine month returned to full duty at own request.

51	Public body	Female telephone operator.	Neurasthenia.	21 days	33 days	Cured	Went to country and resumed work three weeks after leaving hospital.
52	Public body	Female telephone operator.	Neurasthenia and insomnia	54 days	31 days	Cured	Went to country, resumed work four weeks after leaving hospital.
53	Public body	Female clerk.	Neurasthenia.	168 days	77 days	Cured	Went to convalescent home and resumed work (with persuasion) six weeks after leaving hospital.
54	Public body	Female indexer.	Neurasthenia.	35 days	35 days	Cured	Resumed work seven weeks after leaving hospital.
55	Public body	Female ticket checker.	Neurasthenia and neuritis.	40 days	31 days	Cured	Went to country and resumed work 25 days after leaving hospital.
56	Independent	Wife of clerk in public service.	Neurasthenia.	—	40 days	Cured	Three years later continuing in good health.
57	Public body	Female superintendent of domestic subjects.	Extreme neurasthenia. Had been frequently absent during last 16 months.	50 days	26 days	Cured	On leaving hospital went to country for 64 days and then resumed work. To be kept under medical supervision.
			SECTION III.—MALINGERERS (ALL ACCIDENT CASES EXCEPT NO. 11.).				
1	Insurance Company.	Artizan	Alleged inability to straighten knee joint. Question whether functional or malingering. Obviously not anxious to return to work. Much difficulty in persuading him to enter hospital.	254 days	68 days	—	Persistently kept knee flexed in hospital; hospital surgeon diagnosed displaced or cracked internal semilunar cartilage. Malingerer. Died suddenly in hospital from fatty heart. Knee found at post-mortem to be normal, except for slight evidence in *both* knees of commencing rheumatoid arthritis. Knee relaxed on post-mortem table. Flexion had, therefore, been functional.

SECTION III.—MALINGERERS (ALL ACCIDENT CASES EXCEPT NO. 11.)—*continued.*

Number.	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History.
2	Insurance Company.	Labourer	Functional paralysis of left leg and hand combined with malingering.	11 weeks	133 days	Failure	On leaving hospital declined to do any work. Insurance Company settled for £150. Nine months after leaving hospital I was informed that he had made a somewhat remarkable recovery, and for six weeks past had been trying to find work.
3	Public body	Mechanic	Seven years previously had been off work a whole year with strained back. Now having been off work nine months with back again said to be strained was sent to me for examination with a view to superannuation. Sent to hospital.	9 months	11 days	Cured	Malingerer. Told he would be reported as a malingerer and lose pension if he did not immediately resume work. He left hospital and resumed work next day. Six weeks later resumed full duty, and was still doing it 5½ years later.
4	Public body	Driver	Fell against front of vehicle. Obscure pains. No objective signs.	96 days	47 days	Cured	On leaving hospital it was arranged that he should resume work at once, as it is only by prompt action that men of this type can be led to appreciate their duty to themselves and their employers.

							A few months later he complained that he was weak and had pain in his back, that the weather affected it. Examination showed no physical disability. It was pointed out to him that as he had not given notice of his injury a year previously he could not now claim under the Employer's Liability Act; that the alleged accident happened before the Workmen's Compensation Act came into operation; that I believed he never was really ill, and that he was to return to duty forthwith, otherwise he would be dismissed without compensation. He returned to work, and has not complained since of his back or any other part of his body.
A. Y.	5	Public body	Artizan	Alleged pain on top of head as result of blow on head with hammer by lunatic. Seen three months after accident, with healed scar. Idea of injury on mind. Pensionitis.	99 days	11 days	Cured	After a few days in hospital declared himself well and anxious to leave. After leaving declared he was quite unfit for work, and stated he had said he was well and fit whilst in the hospital merely because he wanted to get out! Turned out to be a malingerer, and was made to work under threats of consequences. Subsequently for many months he performed his work in a satisfactory manner, and at outbreak of war in August 1914 left for service with the National Reserve. Died of pneumonia whilst in H.M. Service.

III.—MALINGERERS (ALL ACCIDENT CASES EXCEPT NO. II.)—*continued*.

Number.	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History.
6	Shipping Company.	Mariner	Accident. Blow on head and shoulder. Question of functional neurosis or malingering. Held back persistently stiff.	612 days	45 days	Cured	Malingerer. On leaving hospital returned to sea at once. It transpired that at the time he was sent for by the hospital authorities he was at work in the hop gardens.
7	Solicitor for Shipping Company.	Labourer	Blow on nose and forehead. Traumatic neurasthenia. Had been medically examined by several other medical men, and two years before I saw him had refused offer of 500*l.* in settlement, but subsequently refused to name any sum he would accept. Complained of giddiness; when tested for Romberg's sign he deliberately allowed himself to fall backwards (in obviously feigned manner) when he knew my assistant was behind to catch him.	6 years and 8 months.	42 days	Failure	In hospital no functional or organic disease was found. Three months later examined again, no organic disease, fit for work. Compensation stopped and at arbitration proceedings (a year after leaving hospital) the judge, after hearing medical evidence, gave decision in favour of employers.

8	Solicitor to public body.	Driver	Struck on back in collision with tramcar. Part traumatic neurosis, part exaggeration (if not malingering). Obsession he could not bend back but was induced to do so at examination. Legal proceedings on mind.	269 days	85 days	Cured	At hospital every movement during examination was said to cause pain in lumbar region. Even examination of abdominal reflexes, plantar reflexes, not to speak of knee and ankle jerks, was said to cause him pain in the back. In hospital, although he absolutely refused to straighten back, when turned on his face all curvature disappeared without complaint. Managed a little boxing while in hospital.
9	Public body	Public employee.	Neurasthenia after injury to head.	209 days	105 days	Failure	Resumed work, then relapsed. Certified permanently unfit four months after leaving hospital. Retired with pension of £1 a week. *Very soon after* started work, and at time of inquiry (four and a half years later) was employed at light work. Malingerer.
10	Public body	Driver	Treated for myelitis for 13 months, full pay most of time. Bedridden. Ordered to hospital for observation, where he had "fits," blackening his face to give realistic effect.	426 days	70 days	Cured	Malingerer. Interviewed in hospital. Plain speaking. Next day walked to my house, distant 1 mile. Resumed work within a week.

SECTION III.—MALINGERERS (ALL ACCIDENT CASES EXCEPT NO. 11.)—*continued.*

Number	Employer.	Occupation.	Details of Illness.	No. of Days absent before entering Hospital.	No. of Days Treatment in Hospital.	Results of Hospital Treatment.	Subsequent History.
11	Public body	Agent	Neurasthenia; obsession he had kidney disease.	37 days	50 days	Failure	Resumed work, but relapsed a month after leaving hospital. Six weeks later certified permanently unfit for further service. Retired with pension of £37 a year. Subsequently I came across him in gorgeous uniform in connection with a show; he told me that soon after he got his pension he made a good living by wrestling and boxing. There was nothing physical in this case, but his persistent protestations of weakness and incapacity maintained during the whole time he was in hospital, and his apparent relapse after being sent back to work at the point of the bayonet, ended in his superannuation. At the time, whether he was ill or well, I felt he would be no further use in the public service, and there was not sufficient evidence to report him as a malingerer.

APHASIA AND ITS TREATMENT.

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APHASIA, in one or other of its many forms, is a symptom with which the practitioner is frequently confronted. As a transient or a permanent phenomenon, it may occur in youth, middle life, or old age, and its study is probably better calculated than that of any other cerebral symptom to give the physician an insight into cerebral physiology and physiological psychology. The reader should keep in mind that aphasia is a double-sided condition ; in any case of aphasia two questions arise for consideration, viz., the site and sort of lesion producing the symptom, and the nature of the disturbance of cerebral function thus produced. It is desirable to keep these two questions in view in the study of all cases of aphasia.

Aphasia is itself no disease. It is merely a symptom, the external manifestation of a pathological state of some or other part of the cerebrum. When we speak of different types of aphasia, we do not refer to different varieties of a particular morbid entity, but to certain groups of symptoms, all of which are disturbances of the function of speech—a cerebral mechanism exactly comparable to other mechanisms with which the physician is familiar. To understand the position clearly, we may take a brief survey of cerebral function along general lines.

Physiologically speaking, there are two main systems by which cerebral activity is effected : (1) the projection system, and (2) the associative system.

(1) THE PROJECTION SYSTEM.

The cerebral cortex receives impressions from the sensory surfaces of the body, from certain special sense organs, from the muscles, etc., and despatches stimuli to the voluntary muscles and to various glands. The paths uniting the

cortex to the periphery are known as projection paths or tracts. These afferent or receptive paths and efferent or executive paths are interrupted, at various points, by intercalated stations of grey matter, containing nerve cells, *e.g.*, in the spinal cord. This is true both of motor and sensory projection systems, and of the cranial nerves. On the cerebral cortex certain areas, at which sensory projection paths arrive, or from which motor paths depart, are known as projection fields or areas. Thus the calcarine cortex of the occipital lobe is the projection area of the retina; the transverse gyri of Heschl on the upper surface of the temporal lobe are the projection field of the auditory apparatus; the precentral gyrus is the projection area for the motor cortico-spinal paths, for the motor paths to the motor cranial nerve nuclei effecting movements of the lips, tongue, palate, and so on. These projection fields may be impaired in function either by destruction or by pathological irritation. In the former case, there results paralysis of motion or sensation, as the case may be; in the latter, convulsions, twitching, cramps, and so forth occur on the motor side, and on the sensory, elementary hallucinatory disturbances, pains, paræsthesiæ, and the like, according to the projection field involved.

(2) THE ASSOCIATIVE OR MEMORY SYSTEM.

When a sensory stimulus reaches a sensory projection field, it will produce a sensation, if it is of sufficient intensity. Similarly, a motor stimulus will result in innervation and movement, if it is sufficiently strong. But the brain has another function. All sensory and motor stimuli leave behind them traces or remainders, which facilitate conscious memories of sensations or movements, and, in addition, exist as an unconscious possession of the cortex, enabling it to perform repeated movements more easily and completely. This constitutes the memory system or function, and as these memories from different sense systems are linked up with each other, we get the conception of an associative function of the cortex. The sight of an orange at once awakens visual, gustatory, olfactory, tactile, and possibly other memories of the fruit.

It has long been matter for discussion whether these

memory-associative functions are placed in the projection fields of the corresponding systems, or in their immediate neighbourhood, or independently of them. Without delaying over this subject here, it may be said very briefly that there are large areas of the cortex to which and from which very few or no projection fibres pass; these areas are known as association areas, for they are bound to each other by important groups or sets of fibres which never leave the cerebrum. It is the general view of physiologists and neurologists that the projection fields are concerned both with sensation (or innervation, as the case may be) and the retention of sense-impressions, while the association areas in relation to the projection areas—of which the latter form but a part—are concerned only with the traces or remainders of which we have spoken, and are known as memory areas. The association between memories of the same sort is effected in the cortical area concerned. The association between memories of different sorts or systems is effected by long tracts of fibres passing from one region of the cortex to another. In this view, no part of the cortex is concerned solely with projection.

We have already indicated the disturbances of function produced by lesions of the projection fields. Lesions of the memory-associative regions will disarrange the functions of storing up impressions and fixing their connections.

Now the application to the study of aphasia of this brief sketch of the two main divisions of cerebral function will be at once obvious. Aphasia is essentially the result of impairment of the memory-associative system. Before we proceed to discuss it, however, it may be remarked that the speech mechanism possesses also a projection system, viz., the projection paths from the speech centres, of which we shall learn more immediately, to the muscles of articulation, as well as to the muscles utilized in writing. It is important to note that speaking aloud, and writing-speech, are performed by muscle groups which are used for other purposes as well. Any lesion of the projection systems for these groups will so far interfere with speech mechanism. Lesions of the projection system for the muscles of articulation will produce dysarthria or anarthria, and those of the projection system for the hand muscles cause

inability to write, agraphia or dysgraphia. It is unfortunate, however, that there is no word to express this inability to write from lesions of the projection system, say hemiplegia, as opposed to inability to write from lesions of the memory-associative system. In the case of motor-speech, we have aphasia for associative lesions, and anarthria for projection lesions. In writing-speech, we have no word but agraphia for both.

Anarthria, or dysarthria, then, arises from lesions anywhere on the projection system, from the centres for the movements of lips, palate, tongue, etc., in the motor projection area of the cortex, to the cranial nerve nuclei concerned, and so to the cranial nerves themselves. Further, it may arise from any defect of co-ordination of these muscles from cerebellar disease, or from rigidity of this musculature, without actual paralysis, as in paralysis agitans.

If the cortico-bulbar projection system is intact, and yet the patient cannot speak at all, or not properly, then the condition is one or aphasia. What has gone wrong in this case is our inward speech (*innere Sprache, langage intérieur*), which is something that we have learned, a memory possession, a function of the memory-associative system.

THE ACQUISITION OF SPEECH.

At this point, it is well to clear the ground by a brief sketch of how speech is acquired.

Long ere the child has begun to articulate, its ears have become accustomed to many and varied sounds. Amongst these are the sounds of words. At first, words are to the child mere sounds, without any meaning. Some of these sounds are repeated in his hearing much oftener than others, so that when he is still not many months old he is already learning to distinguish them. Very speedily he comes to associate these special sounds with certain objects; thus, the earliest established path in his acquisition of inner language is the association of a certain sound with the ideas of objects. The next step is the endeavour to imitate by articulation the sounds he hears constantly repeated by others, and in this fashion he at the same time acquires a store of memories of the movements necessary for the articulation of these sounds, or words. Before he ever learns to read or to write,

therefore, his inner language consists of the memories of the sounds of words, closely linked to the memories of the movements for words. It is the former of these two groups that is the more intimately bound to the ideas of objects, for which the words appear to be the representatives. There is, however, a less strong and less complete association between the idea of an object and the memories of the movements for the corresponding words.

When his nurse says "bow-wow" he will think of his little toy dog, look for it or point to it, and when it is shown to him he will say "bow-wow." Thus as early as he begins to think at all, he is developing his inner language. The coin of his little realm of thought consists of auditory and motor (kinæsthetic) memories; underlying these is an actual, a material—though unconscious—possession consisting in the physiological linking of various groups of innervations, of which only those corresponding to the former, auditory, memories have a psychical equivalent.

When he reaches the stage of learning to read and to write, his inner language becomes considerably more complex.

He learns to write by letters and syllables; these are the signs for sounds, be it noted, for our writing is phonetic. It can thus be understood that writing-language is connected with what has been termed the "ideational centre" through the medium of the centre for the memories of the sounds of words. Corresponding to these sounds is a visual picture for each, made up of a letter or letters, and in this way a visual centre, or rather a centre for visual language, is gradually developed, composed of the visual memories of letters, syllables, and words. Finally, the use of the hand and arm muscles for the reproduction of these signs and sounds results in the storage, in a writing-language centre, of the memories of writing movements—a kinæsthetic centre analogous to that for spoken-language.

Once this more elaborate inner speech mechanism is established, its action, physiologically speaking, must be somewhat as follows:—

In speaking, the idea of a word or words, awakened in the "ideational centre" already referred to, arouses the corresponding auditory word memory, thence the kinæsthetic motor

memory, thence the cortical projection centre in the motor area proper (precentral gyrus), and so the tongue, etc., perform the necessary movement.

In writing, the stimulus from the "ideational centre" passes to the auditory centre (and probably also to the kinæsthetic motor centre); from both of these it passes to the visual word memory centre, thence to the kinæsthetic writing-memory centre, and so the muscles of the hand are innervated.

Similarly, on the receptive, as opposed to the executive, side, the stimulus proceeds, for the understanding of spoken language, from the ear to the auditory projection centre, thence to the allied auditory memory centre, and so to the "ideational centre." For the understanding of written language, the route is from the eye to the visual projection centre, thence to the visual memory centre, thence to the auditory memory centre, and thence to the "ideational centre."

In this brief description reference is made to "centres" in a fashion that may perhaps convey a wrong impression. There are indeed projection centres—areas—which may be exactly delimited, as in the case of the visual area in the calcarine cortex, the motor area in the precentral cortex, and so on. But when we speak of associative centres, for lack of more precise anatomical knowledge we are obliged to speak physiologically; they are to be understood, therefore, as indicating the focus of functional activity of the particular system concerned. As already hinted, we are not precisely certain that the anatomical basis of such foci is in the projection centre that corresponds, or overlapping it, or apart from it though in its vicinity. Still more is this true of an "ideational centre." This is quite hypothetical; ideation may be a property of the whole of the cortex, but the fact remains that in speaking, the idea of a word precedes its enunciation, and for convenience sake we postulate a "centre" where these ideas are aroused. That it is in any anatomical sense a separate "centre" is more than problematical.

The reader will therefore see how unsatisfactory are the various schemata devised by the ingenious to simplify and organize the complexity of the cerebral speech mechanism. The plotting out of physiological centres on paper almost

inevitably leads to the conviction in the student's mind that they stand for anatomical areas of the cortex, which is far indeed from being the case. The drawing of lines of communication between these physiological centres and a psychical or ideational centre, distinct from them, makes confusion worse confounded.

When this protest has been entered against such graphic anomalies, nevertheless it remains profoundly true, clinically, that there are differing types of aphasia, differing aphasic symptom-complexes, which, always considered clinically, can readily be explained as affections of different parts of the speech mechanism, however difficult or impossible it be to correlate the symptoms with the underlying pathological defect. Clinical differentiation is at present far in advance of pathological identification.

THE CEREBRAL LOCALIZATION OF SPEECH.

If we now endeavour to transfer our physiological scheme of how the speech mechanism works to its place in the brain, as it were, we meet at once with the striking fact that in right-handed individuals it is the left cerebral hemisphere that is mainly concerned with the function of speech. Over the explanation of this remarkable phenomenon we shall not delay. That the right hemisphere to some extent may partake, in normal subjects, in the function of speech is probable, but of the fact that the left hemisphere leads the right there can be no doubt.

In this left hemisphere, then, there is unquestionably a "speech area," lesions in any part of which site are followed by one or other clinical variety of aphasia in an overwhelming number of instances. The exceptions only prove the rule. Both cortex and subcortical fibre-systems are to be regarded as included in the area, which may be taken to consist of the lower and posterior part of the frontal lobe, the island of Reil, the part of the precentral gyrus that overhangs the island of Reil (operculum Rolandi), the posterior part of the temporal lobe, and a section of the parietal lobe in its lower part.

In thus describing the speech area of the left hemisphere, it is important to realize at the same time that, owing to the

linking up of neuronic systems, lesions outside this area may indirectly disturb functions there focussed, so that the field in which, directly or indirectly, lesions may cause aphasic disturbances is perceptibly widened. The speech area as above defined, however, is for practical purposes sufficiently definite.

CLINICAL TYPES OF APHASIA.

The next point that arises is: are there subdivisions of speech function in this area, of such a kind that lesions in one part always produce one type of aphasia, lesions in another part another type? The student of the subject knows that, in this regard, differences of opinion exist. It is accepted by most, however, that lesions in the frontal section of this speech area, including the anterior part of the island of Reil, occasion speech impairment of a motor type, whereas lesions in the temporal and parietal section give rise to aphasia of a sensory type. We may look at these a little more closely.

I. Without specifying more exactly the cortical and subcortical area involved in the first of these two types—for it appears to vary to some extent with the individual—a lesion there situated occasions loss of the motor components of words, *i.e.*, the patient cannot find, or arouse, his motor memory images of words. He is accordingly dumb, or at most has only a few words or parts of words. He cannot repeat words on request, and he cannot read aloud. We have seen that the physiological path for writing passes through this kinæsthetic motor centre, in most individuals, hence he cannot, as a rule, write spontaneously or to dictation: he can copy, however, for in the process this centre is not implicated. Such is the clinical picture of complete motor aphasia.

II. In the second type, the patient cannot remember the meanings of the sounds of words, nor the tones of words (letters and syllables included). He hears sounds and tones, but does not know that they are words. He is word-deaf. Since the auditory components of spoken speech are of fundamental importance, as we have seen, he has difficulty in speaking; from defect of these auditory components he makes mistakes in words, syllables and letters—known as paraphasia. A severe degree of this constitutes jargonaphasia. Owing to the dependence, further, of both writing and reading on the

integrity of the auditory word centre, as we have seen, he makes similar mistakes in writing to those of his speaking—known as paragraphia. In the same way he makes mistakes in reading—paralexia : sometimes it, the defect, is greater—dyslexia : it rarely amounts to complete alexia. He has the same difficulty in understanding what he reads as what he hears.

This is the clinical picture of complete sensory aphasia, and it is readily separable from motor aphasia.

III. Complete or total aphasia, from a lesion (usually of the Sylvian artery and its branches) involving both frontal and temporo-parietal sections of the speech area, is quite common ; a complete or almost complete motor and sensory aphasia. The motor aphasia usually masks the sensory side of the complex. There is always a tendency for the word-deafness to diminish in degree, presumably from the development of a corresponding subsidiary centre in the right hemisphere, so that in old cases of originally complete aphasia the motor element certainly predominates.

IV. Attention has been more directed than formerly to lesions between the frontal and the temporal divisions of the speech area, lesions of the island of Reil, and an "island-aphasia" (*Inselaphasie*) or, rather, varieties of aphasia have been described. A lesion of the island of Reil is apt to interrupt a number of the fibres of association binding the auditory and the motor memory centres ; such, at least, is what may be deduced from the type of aphasia produced. It approximates to the motor variety. Spontaneous speech is much impaired, and the repetition of words on request, to a less extent ; there are as well paragraphia and paraphasia.

V. We may next refer to a minor degree of complete motor aphasia, known as pure (or subcortical) motor aphasia, and a minor degree of complete sensory aphasia, known as pure (or sub-cortical) word-deafness.

The former consists in the impairment or loss of spontaneous and repeated speech only ; reading and writing are intact ; it is pure "word-dumbness." There has been considerable discussion as to the explanation of this clinical variety. According to Liepmann, the majority of individuals, more especially the less well-educated, spell the words

inwardly as they read and write; others do not use their motor speech memories either in reading or writing. Should any of this latter group have a lesion of their motor speech centre, in the anterior part of the speech area, it will not be associated with either writing or reading difficulties. It will be pure word-dumbness.

In others, again, the clinical picture is found where the motor speech centre is itself intact or almost intact —hence utilizable for writing and reading purposes—but where there is a cleavage or dissociation between that centre (associative system) and the projection system of fibres that go down to the appropriate pontine and medullary motor nuclei. The term subcortical is misleading in this connection, and should be abandoned. This variety is, in a sense, intermediate between aphasia and anarthria, and if its physiological explanation is a little difficult, there is no doubt of its clinical occurrence.

VI. Pure word-deafness consists clinically of inability to understand spoken speech: as a natural corollary, the patient cannot repeat words to order and cannot write to dictation. Otherwise, his inward language is intact. He can speak, read, write, and copy. As opposed to complete sensory aphasia, there is no paraphasia, paragraphia, or paralexia. There is a dissociation of the memories of the sounds of words from all other sounds, while the centre for auditory word memories is intact; hence, the patient cannot distinguish word-sounds from other sounds, and is word-deaf, but his auditory word memories are utilizable for reading, writing, and speaking. In fact, as in pure word-dumbness, there is a dissociation between the projection system and the associative system concerned. Needless to say, before making the diagnosis one must be sure that the patient's actual hearing is unimpaired. Subcortical lesions in the temporal part of the speech area have been shown to produce this variety of aphasia.

VII. There is a further variety of aphasia, known as transcortical, which may be either motor or sensory or combined. The reader should understand clearly that the term transcortical is now being used by the writer solely in a clinical and symptomatological sense, *i.e.* to designate the

cases in which there is defect in the speech mechanism of a higher type than those hitherto considered.

In transcortical motor aphasia, the patient cannot speak spontaneously, though he can say anything to order correctly. He cannot write spontaneously, but copying and writing to dictation are unimpaired. One of the conditions under which it occurs is when the anterior part of the speech area is involved in a lesion, which is sufficient to prevent the awakening of words spontaneously in the motor speech centre from volitional stimuli, but insufficient to hinder their awakening from the stronger stimulus of the words pronounced by someone else in the patient's hearing. A variety of transcortical motor aphasia is often seen, too, in abscesses of the temporal lobe secondary to ear disease. In such cases, the patient has great difficulty in "finding his words" (so-called amnesic aphasia or verbal amnesia), especially substantives and verbs. Once the word is given him, he instantly recognizes it, repeats it, and uses it correctly. That is, what he cannot well say voluntarily, spontaneously, he can say on receipt of adequate sensory stimuli from without.

VIII. In transcortical sensory aphasia, on the other hand, the auditory memory centre is isolated from the so-called ideational centre. Put in a less controversial way, the patient has lost the meanings of words; he hears words and knows that they are words, but the sound of a word, reaching his auditory memory centre, does not awaken the meaning of the word, the concept for which it stands. Hence, the path to the motor speech centres being open, he often repeats what he hears correctly, not knowing what it means. Similarly, he can read aloud, can write to dictation or copy, without knowing the meaning of what he reads or writes. There is rarely spontaneous speech, so that transcortical sensory aphasia is frequently associated with transcortical motor aphasia; the patient repeats like a parrot what he hears. As a result, such patients are often thought to be demented; the most perfect instance of this variety that the writer has seen is in an asylum patient, legally but not medically insane. In severe atrophic lesions of the temporal lobe the syndrome is prone to occur.

IX. There remain for very brief mention isolated disturb-

ances of writing-speech—pure alexia and pure agraphia.

Deep lesions under the parietal part of the speech area may cause pure alexia, accompanied or not by hemianopia. The explanation is that the visual stimuli from words seen do not pass, owing to the lesion, from the visual projection centre to the visual memory centre ; hence, they do not reach the auditory word centre, to awaken the sounds of the words, and, consequently, the patient cannot read.

In pure agraphia a lesion interrupts the passage of stimuli from the visual word memory centre to the kinæsthetic writing centre.

RELATION OF APHASIA TO AGNOSIA AND APRAXIA.

If we take a summarizing view of these affections of the speech mechanism, both receptive and executive, we should have no difficulty in appreciating the significance of the data when envisaged from another side. Word-deafness and word-blindness are defects of recognition ; the patient sees and hears, but he does not understand. There is no paralysis of his projection centres, but only of association systems. Now there are other defects of recognition than those concerned with words. He may see objects, but may not recognize them by sight. He may taste, smell, touch objects, but fail to recognize them by these sense avenues. He may fail to recognize by one avenue, but succeed by another. The general name now given to the symptom of failure to recognize, by any sensory system, is agnosia. Thus we may have visual, tactile, auditory, gustatory, olfactory agnosia.

The reader will at once see that word-deafness is a variety of auditory agnosia : it is agnosia for the *sounds* of words. Transcortical sensory aphasia is agnosia for the *meanings* of words. Word-blindness is agnosia for writing-signs. On the executive side, the patient with motor aphasia has no paralysis of the muscles of his lips, tongue. palate, etc., but he cannot speak. In agraphia, there is no paralysis of the small muscles of the hand, but he cannot write. The term now used for inability to perform certain acts, where no paralysis prevents their execution, is apraxia. Looked at in this way, motor aphasia is apraxia of the lips, tongue, palate, etc., for the movements of speech. Agraphia is apraxia of the arm and hand for the

movements of writing. Aphasia and agraphia may thus be and not infrequently are, part of a larger apraxia, *i.e.*, apraxia for other movements besides those concerned in speech. Sensory aphasia may be, and often is, part of a larger agnosia, *i.e.*, an agnosia for other things than words.

It is well that the reader should grasp the advantages secured by regarding motor and sensory aphasia as parts of wider cerebral symptom-complexes, viz., those of apraxia and agnosia. It serves to remove any lingering idea as to the individuality or uniqueness of aphasic symptoms as opposed to other higher cerebral symptoms; it paves the way for a more comprehensive conception of cerebral activities, both afferent and efferent.

THE TREATMENT OF APHASIA.

We may turn from these matters of symptomatology and physiological psychology to consider concisely the question of the treatment of aphasia.

When the practitioner is faced with a case of aphasia it is often difficult to say what the outlook really is. Some severe cases clear up unexpectedly, others, slight from the beginning, remain uninfluenced. In the endeavour to give an accurate prognosis, the following considerations are worthy of attention.

(1) It is true, as a general rule, that the more advanced the age of the patient at the onset of aphasia, the less likely is improvement to occur. Nevertheless, there are well marked exceptions to this rule. Some children, after an encephalitis causing aphasia, never make that improvement which we expect; and some old folk make a rapid recovery. In this connection a further consideration must be mentioned; the longer the interval between the stroke and the reawakening of speech, the less likely is the improvement to be material. To this generalization the writer attaches much practical importance.

(2) Still more depends on the severity of the original attack. In a large class of case the aphasia may be regarded as strictly transient, and in these the prognosis naturally is good. Reference is here directed to certain attacks of Jacksonian epilepsy, migraine, cerebral arteriospasm, incomplete thrombosis or endarteritis obliterans, certain toxic and

toxi-infective conditions, congestive attacks in general paralysis, etc. In such cases the aphasic disturbance may clear up entirely in a very short period. It is well, on the other hand, not to forget that transient aphasia from cerebral vascular disease may become permanent if an ictus occurs.

In an elderly patient with aphasia definitely established, the following points may be put before the physician as worthy of remark.

(*a*) If there is little or no indication of generalized cardiac, arterial, or renal disease, the outlook is better than if such systems show signs of degeneration.

(*b*) Should the aphasia be unaccompanied by any paralysis, facial, brachial, hemiplegic, etc., the chances of improvement are better than otherwise. Palsies are simply an indication of the degree of the lesion, and the larger the lesion, the less likely is improvement to take place.

There is evidence to show that some cases of aphasia improve because of functional restitution in parts of the brain damaged but not destroyed by the lesion. In other instances, the evidence suggests that auxiliary speech mechanisms develop in undamaged areas of the cerebrum, a condition of functional compensation.

In all cases of aphasia, treatment should be directed along two lines,—

(1) The treatment of the causative morbid process, and

(2) The treatment of the symptomatic condition once it is established.

(1) The common causes of aphasia are embolism, hæmorrhage, thrombosis, inflammation, and tumour. Whenever the physician has made his diagnosis of the underlying mischief, he should prosecute treatment actively. It is unnecessary to indicate in this article the appropriate measures to be adopted in each of the above forms of intracranial disease.

(2) Treatment may have to be directed to the restoration of speech by functional compensation. A number of cases have now been recorded in which the organs of speech were re-educated *de novo*, with excellent results. As the writer has said elsewhere, "the evidence favourable to the re-education method is ample enough to render its comparative neglect by the profession rather inexplicable. Naturally, in order that it

may be prosecuted to a successful issue, the combination of a suitable case, a diligent pupil, and an enthusiastic and patient teacher is almost a *sine quâ non*, and doubtless such a combination is not always to be found. Yet even a modicum of success is worth striving for, and it may be hoped that henceforward the physician will address himself to the task with greater devotion and assiduity."

In all cases, the method is essentially one of imitating the procedures by which a child first learns the elements of speech. In order to give the reader a practical acquaintance with methods in vogue, one may be allowed to cite *in extenso* the technique of Dr. Charles Dana, of New York.

"(*a*) Repeat five exclamatory words, such as 'ah,' 'oh,' or other exclamations expressing joy, anger, or other emotions. Repeat after teacher ten monosyllabic nouns or pronouns. Repeat ten polysyllabic nouns. Repeat ten verbs. Each time a noun is named, let the patient see the object, feel it, and see the written or printed name on a piece of paper before him, thus stimulating visual, auditory, and tactile memories at the same time.

"(*b*) Repeat the letters of the alphabet, these letters being held in front of him. Repeat letters of the alphabet after writing and looking at each one. Repeat the numerals from 1 to 20. Repeat them while looking at the figures. Write and repeat the figures.

"(*c*) Repeat ten simple qualifying adjectives, such as white, black, red, smooth, soft, rough. At the same time, let him see the object and colour, or feel the same.

"(*d*) Later, let him try to repeat sentences of three words, in which the noun is joined to the adjective, *e.g.*, 'book is red,' 'box is white,' etc.

"(*e*) If the patient has any musical capacity, sit him at a piano and hum the notes of the piano, going through an octave, and then let him try to hum a tune, striking a note at the same time. Finally, teach him to sing the tune through, and then introduce the possible words. Some patients can sing before they can talk.

"(*f*) Copy sentences made up of the words he is being taught. Let him have an ordinary copybook and have the copy at the top of the page. Let him fill a page every day,

trying at the same time to pronounce the words as he writes them. Have him copy first the familiar nouns, and then the simpler verbs, then the simple adjectives: finally, let him copy sentences. Take a small vocabulary, and repeat from this, not trying to enlarge too soon.

"(*g*) Write the letters of the alphabet and as the patient writes them get him to try to repeat them. Do this without a copy, if possible. Then let him write words to dictation, using the same vocabulary above referred to. Finally, let him try to write short sentences to dictation, then try to read them after he has written them, with assistance at first, then without.

"(*h*) Write numbers 1 to 20, and say them out loud when written.

"(*i*) The patient should allow himself to be read to for a short time twice a day, and he should try also to repeat a quarter of a page every day."

Another method is a more strictly phonetic one, and consists in teaching the patient the letter-sounds of each vowel and consonant. A combination of this procedure with lip-reading is often of value in motor aphasia. The patient is shown by direct lip-reading how to place the lips, tongue, etc., for the pronunciation of each letter-sound.

What has been said hitherto has a bearing rather on the treatment of motor than of sensory aphasia. It has been held that the latter variety is more difficult to treat successfully, *i.e.*, that once sensory aphasia is established, improvement under treatment is less likely to occur. In a case of word-deafness, for instance, the aim of the teacher, physiologically expressed, is to develop an auxiliary auditory word centre in the right hemisphere and to bring it into functional relation with the motor speech centre in the frontal part of the left hemisphere speech area. In word-blindness similar lines of attack are indicated. The reader can understand that work of this sort entails the expenditure of much time and patience, but in cases that have come under the writer's own observation, and in certain recorded cases, extremely good results have been obtained. The tactics pursued are somewhat as follows:—the patient first of all learns the alphabet, attention being concentrated on each letter in turn. As this is being done, the

teacher pronounces the letter. Eventually the patient names the letters himself, being taught also by lip-reading to do so. Thus afferent impressions from more than one sense avenue are being utilized together. The next step is to tackle monosyllabic words, which the patient learns to spell out letter by letter, while the teacher pronounces each letter and the word as a whole. Again he utilizes the lip-reading method to assist the patient as the latter endeavours to read the word aloud. A number of short lessons during the day are better than one long one.

It is frequently observed that aphasic patients are peculiarly apt to speak in the "telegram-style," omitting parts of speech which may not be necessary for comprehension but are, nevertheless, essential for correct speaking. It is more particularly prepositions and articles which are omitted, and nothing really shows the poverty of the patient's language so much as their omission. The teacher should apply himself strenuously to get the patient to reacquire these all important articles, conjunctions, prepositions and auxiliary verbs, from the outset. In a word, the grammar of language has to be learned again, as it was learned at school.

RECENT WORK IN OPHTHALMOLOGY.

By L. V. CARGILL, F.R.C.S.

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A HOPE was expressed in my last review on ophthalmolgy (THE PRACTITIONER, October, 1913) that the notification of ophthalmia neonatorum would soon be compulsory throughout the United Kingdom. From 1st April, 1914, the Local Government Board extended the compulsory notification to every sanitary district in England and Wales, defining the complaint as "ophthalmia with a purulent discharge from the eyes of an infant commencing within 21 days from the date of its birth." It is worthy of record that, in 1884, a special Committee of the Ophthalmological Society of the United Kingdom [1] recommended that a card of printed instructions should be read and handed to each person registering a birth. On each card was to be printed the following :—"If the child's eyelids become red and swollen, or begin to run with matter within a few days after birth, it is to be taken without a day's delay to a doctor. The disease is very dangerous, and if not at once treated may destroy the sight of both eyes." If the Local Government Board had acted on that recommendation, the sight of many people now blind would have been saved.

Before the Ophthalmic Section of the last International Congress of Medicine, J. M. West [2] read a paper on "An Intranasal partial resection of the lachrymal sac for cases of Dacryostenosis after an experience of 135 operations." "West's operation," as modified by Halle and recently performed by Graham and Paton,[3] consists in dissecting up a squarish flap of mucous membrane from the outer wall of the nasal fossa in front of the anterior end of the middle turbinal; chiselling away the bone over the inner wall of the lachrymal sac; passing a probe horizontally inwards along the lower canaliculus so as to bulge the inner wall of the sac through the gap made in the bone; perforating the bulge, from the nose, with the galvano-cautery; replacing the flap of nasal mucous membrane; and then again, by means of the bulging caused by the

probe, burning a hole in the flap corresponding to the hole in the inner wall of the sac. The operation is done under local (cocaine adrenalin) anæsthesia, a style wire is left in the aperture, during healing, and the nose is plugged; subsequently, boric lotion is syringed through the canaliculus for some days until the fluid comes away clear.

By this means, an opening is made from the sac into the nose, and the epiphora, dacryo-cystitis, fistula, and other results of a complete stenosis of the nasal duct are cured. Painful, uncertain, often barbarous treatment with probes is avoided, and there is no skin incision as is the case in excision of the sac or in Toti's operation. Some critics have objected, on the score of infection, that the lachrymal sac is converted into part of the nose; and others have thought that blowing the nose might cause surgical emphysema; but the reports of cases are excellent. Purulent mucoceles have quickly been cured, with the result that in some cases cataracts have subsequently been removed successfully.

The operation is of course contra-indicated when the canaliculus is occluded, and when the nostril is contracted by scars, as well as in the very young or very old. In one case, however, Graham removed the nasal septum to gain access. West's operation is well worth a trial in troublesome cases of lachrymal obstruction.

I am accustomed to warn students against making a hasty diagnosis of cataract before proper examination with transmitted light, and, when the condition of lens opacity is determined, to discriminate between those cases of broad, grey, ill-defined, coalescing and progressive striæ, and those with sharp, dark striæ which are almost stationary; also, to avoid using the term cataract to a patient so long as the visual acuity is not seriously affected by the lenticular opacity.

In a paper on "The prognosis in incipient cortical opacities of the lens," Jessop[1] has called attention to the class of case in which progress of the opacity is extremely slow, the striæ being thin, fine, short and discrete, and situated peripherally in the superficial layers of the cortex. In the discussion which followed, it was suggested that the term cataract should only be used to patients when there was progressive and serious impairment of vision, which would require early

or comparatively early operation. Sir Anderson Critchett mentioned the case of a patient who, having been told at the age of 48 that he had cataract, became so apprehensive that he insisted on an examination every few months, and yet lived to the age of 86 with good sight. Other ophthalmic surgeons could doubtless narrate similar cases.

The appellation "Dermogenetic" has been given to cataract[5] developing in early life in association with extensive skin disease such as eczema, furunculosis, and erythema exudativum. Auto-intoxication is the probable cause, although embryonic affinity is also suggested. The development is rapid, but without complications. The changes, beginning in the capsular epithelium, lead to stellate opacity in the anterior cortex, and the development of triangular sectors of opacity.

The subject of glaucoma has continued to attract considerable attention and discussion, and probably more has been written on the subject in the last year or two than ever before, since Graefe's classical introduction of iridectomy as a curative measure in 1856. Whilst sclerectomy (or keratosclerostomy, as perhaps it would more accurately be described) by trephining at the sclero-corneal junction, after the reflection of a conjunctival flap, is now largely adopted for glaucoma, and particularly for chronic cases, there are distinct evidences of some reaction against the initial excess of optimism derived from the excellent results which were obtained.

Cases of late infection after trephining have been reported by Axenfeld and others.[6] The cushion of conjunctiva over the trephine hole sometimes exhibits a kind of rarefaction or thinning, resulting in a pale, prominent, almost transparent vesicle, which must be very vulnerable to injury or ulceration. In cases of panophthalmitis, reported as occurring a few weeks or a few months after operation, the conjunctival cushion has been found ulcerated, or a minute fistula demonstrated by fluorescin.

Another of the possible disadvantages of trephining, to which attention has been directed, is the sudden, prolonged or permanent hypotony[7] which may result. This excessive lowering of intraocular tension may lead to thrombosis or hæmorrhage, owing to loss of support to degenerate blood-vessels.

According to Treacher Collins, the patency of the iris-free

sub-conjunctival fistula, which is obtained by trephining, is maintained on the one hand by the conjunctival flap, which prevents any plugging with conjunctival epithelium, and, on the other hand, by a sufficiently large aperture in the endothelial lining of the anterior chamber to prevent the gap being bridged across, whilst the substantia propria being bathed in aqueous behaves like the cut edges of an iridectomy coloboma, and does not form granulation tissue.

Herbert [8] is of opinion that the true filtration of sclerotomy will, in the long run, be found to give better results in cases of glaucoma with useful vision than the fistulization of sclerectomy. Ducamp [9] has described the microscopical appearances at the site of trephining performed with a 2·5 mm. instrument in the eyes of four cats. The trephine hole became blocked by vascular fibro-cellular tissue, and Descemet's membrane had been merely incised, and not excised. In only one of the cases was fistulization obtained, and that was merely temporary and due to a little tag of sclera which had escaped the trephine. His opinion is that cicatrization takes place unless it is prevented by heterogeneous tissue, *e.g.*, iris. Supposing this to be true, we gained this effect by means of the old iridectomy, in which a conjunctival flap was cut with a Graefe knife, and a small tag of iris left in the angle of the wound.

Ellett [10] trephined 12 rabbits' eyes, and enucleated them subsequently at varying intervals. In one eye, removed three weeks later, there was a subconjunctival cyst; in another, removed at the end of two months, subconjunctival tissue bridged the aperture, and in the rest, removed later, new tissue had appeared which was as impermeable as the adjacent corneosclera.

In regard to this experimental work, it must be pointed out that the anatomical conditions in these animals differ from those in man, whilst the patency of the trephine hole is often obvious to inspection long after the successful trephining of a human eye.

Risley,[11] is of opinion that, as glaucoma is the ocular manifestation of a general toxæmia with a local infection, preventative treatment should be directed to these factors. But when the increased tension is established, he is old-fashioned enough to consider that a peripheral iridectomy is the best means of freeing the adhesions at the angle of the

chamber and arresting or warding off the results of increased tension.

Abadie [12] raises a warning note against the many operative procedures which are being introduced, inspired mainly by the theories of their inventors, and the number of which proves that none of them are quite satisfactory in all cases. He maintains the old standpoint that, in chronic simple glaucoma, the judicious and prolonged use of eserine should be tried first, and that only when it fails should iridectomy be done, whilst sclerotomy or trephining should be reserved for cases in which iridectomy has been unsuccessful. He mentions the unsuccessful operations performed by several (*sic*) surgeons on a distinguished colleague, whose chronic passive glaucoma had been retarded or checked for 13 years by myotics. He records, too, the case of another ophthalmic professor with the same disease, who continued working satisfactorily until his death, 10 years after the performance of simple iridectomies.

Cases of simple glaucoma, kept under control by myotics for a considerable time, are not uncommon, and a hospital case, which was so treated and watched for 13 years, has been the subject of a recent paper. In addition to the local treatment, the general condition of the patient must receive proper attention in all cases.

There is great variation in the technique of trephining, as done by different surgeons. Some people prefer the 2 mm., others the 1·5 mm. trephine; some do not touch the iris unless it prolapses, others incise it radially, or do a small basal iridectomy, whilst there are some who include the whole width of the iris in the iridectomy. Elliott [13] himself now advocates the 2 mm. trephine and a basal iridectomy as a routine measure. He trephines in such a manner that a hinge is left on the scleral side of the disc, so that when the trephine is withdrawn, the disc is pushed up by a small knuckle of iris; then, with fine forceps, the disc and iris are seized together and divided simultaneously with a snip of the scissors. All risk of dragging on the iris is thus avoided, and the seizure of the disc serves to steady the eye.

Dupuy Dutemps [14] dissects the conjunctival flap upwards from the corneal margin, and, after trephining at the limbus, refixes the flap at each end. Hill Griffith [15] recommends, and has found satisfactory, the following method. Using a 1·5 mm. trephine,

he places it without previous interference with the conjunctiva, so that one-third of the cutting circle is in clear cornea. He gently draws out and snips off the prolapsed iris; and closes the opening by one fine suture in a horizontal direction. The complete absence of a conjunctival flap, and the presence of a suture just over the trephine hole, would not recommend themselves to one who believed in the expediency of sub-conjunctival trephining.

Brookbank James[16] has again called attention to his method of operating. After turning down a large conjunctival flap, by gradually cutting into the anterior chamber at the sclero-corneal junction with a Graefe knife, he isolates a small wedge of sclera, performs an iridectomy, and turns the scleral tag out under the replaced conjunctival flap. The Reviewer is of opinion that this operation has not received the notice that its merits deserve, for, as James has already pointed out, there is excellent control during the whole operation. The aqueous can be tapped, and tension lowered very slowly; the iridectomy can be performed easily, painlessly, and satisfactorily without the risk of entanglement, and filtration occupies the length of the wound, instead of being limited to a small area covered by a thin vesicle of conjunctiva.

I have frequently operated according to this method, and in some cases, for the sake of comparison, I have in the same patient trephined one eye and done this operation on the other. The knife is more under control even than the trephine, and a satisfactory reduction in tension is obtained without undue hypotony, and with a slightly raised, diffuse area of œdematous conjunctiva, instead of a thin, localized, vulnerable, vesicle-like elevation.

Attention has been called to an hereditary affection in which blue sclerotics are associated with brittle bones and a peculiar liability to fractures and sprains.[17] The probable cause is general defect of the mesoblastic tissues of the body, the blueness of the sclerotics being due to a deficiency in the fibrous tissue, and the bones being more transparent than the normal towards their extremities with defective fibrous tissue about the joints. Affected members of a family are usually small in height and weight, the unaffected members being up to the average.

Stargardt[18] has described a type of familial neuropathic

eye disease, which is evidenced by a progressive macula, degeneration commencing in both eyes, rather suddenly, at about 12 years of age, with a central scotoma, first for red and green and then for white, the fields being normal peripherally. Progress is about equal in the two eyes, and periods of quiescence may alternate with periods of further progress; but, although central vision may become so damaged that ordinary reading is impossible, it does not terminate in blindness. The Wassermann test is negative. The ophthalmoscope shows, at first, irregular pigmentation at the macula with yellowish grey spots and, later, white spots with pigment "like osteoblasts," which eventually coalesce to form an oval patch with its long axis horizontal.

Cases have been reported of a peculiar degeneration and dystrophy of the cornea occurring in tabes,[19] [20] in association with Argyll Robertson pupils and optic atrophy. The corneæ exhibit dull, mottled-looking areas, consisting of innumerable, small, ill-defined, greyish dots, lying in the deepest layer of the cornea, and developing without any inflammatory symptoms.

Evisceration instead of enucleation is usually performed in cases of panophthalmitis, and is generally considered to be free from the risks of septic meningitis, due to infection of the optic nerve sheaths. The report, therefore, of a death[21] from purulent meningitis, three days after an open evisceration for panophthalmitis, is noteworthy. The infection had reached the meninges along the optic nerve, for this was found injected and considerably swollen, and a bead of pus exuded from its cut surface at the optic foramen.

The success of Noguchi in obtaining pure cultures of the spirochæta pallida, from which an emulsion, named by him "Luetin," can be prepared, has made possible the diagnosis of syphilis by a skin reaction, on the same principle as the tuberculin reaction and the mallein test for glanders. The emulsion is prepared by grinding up solid media rich in spirochætes, and fluid cultures of different virulent strains, in an agate mortar, then placing in a water bath at 60° for an hour, adding 0·3 per cent. Trikresol, and ensuring sterility by cultivation and animal inoculation. This is mixed with an equal volume of normal saline, and 0·07 c.c. is injected intradermically on the outer surface of the arm, after purifying

with alcohol and ether, or sublimate. The positive reaction of a specific hypersensitiveness, or anaphylaxis, is evidenced by a large, raised, reddish, indurated papule, which appears in the course of from 24 to 48 hours, increases during 3 or 4 days, and disappears in about a week with or without pustulation. In a few cases, the reaction may fade away in 3 or 4 days, whilst in others the reaction may light up and even pustulate after 10 days. In negative cases, there is, in about 24 hours, only slight temporary hyperæmia devoid of induration.

According to Browning's experience[22] of this Luetin test in 100 cases, it would appear that it is a simple and reliable test within the reach of all practitioners; that it is more delicate than the Wassermann reaction in such cases as interstitial keratitis, choroiditis, and tabes; that it is useful in deciding a doubtful Wassermann reaction; that it is superior to the Wassermann test in proving whether the patient is cured; and that it is of great value when syphilis is complicated by malaria or other protozoal disease.

From the results of 200 cases of ocular syphilis treated at the Lariboisière with salvarsan and neo-salvarsan,[23] it has been concluded that they are chiefly efficacious in acute uveal affections of the anterior segment of the eye, particularly in those of recent syphilis. Ocular tabes, retinal affections, and interstitial keratitis are but little amenable. Neo-salvarsan was found simpler, safer, and more satisfactory, and has been given latterly in only 1 to 2 ccc. of fluid by means of a Roux's syringe.

For the treatment of that serious and frequently disastrous pneumococcal ulceration of the cornea known as ulcus serpens, excellent reports have been made of the efficacy of ethyl-hydrocupreine hydrochloride (syn. optochin hydrochloride),[24,25] a white crystalline powder introduced by Morgenroth. Cupreine is an alkaloid allied to quinine, and found with it in cuprea bark. Ethyl-hydrocupreine hydrochloride has a powerful action on cultures of pneumococci, and on the pneumococcic septicæmia of mice. The negative results obtained in human pneumonia is believed, by Sir Almroth Wright, to be due to the rampart-like protection of the germs by the coagulated lymph in the pulmonary alveoli. The best way of using the drug for the corneal ulceration is by the application of a 1 per cent. solution on a small saturated

cotton-wool swab, cocaine being previously instilled to diminish the pain and burning caused by the application. A stronger solution than 2 per cent. has a caustic effect, and should not be used. The application should be made with a little pressure, until there is a slight opacity around the ulcer.

Instead of this topical application, a 1 per cent. solution has been dropped into the eye hourly, and continued until the ulcer became clean and free from infiltration, generally in the course of two or three days.[26] After the subsidence of pain from the first instillation, an anæsthetic effect remains and lasts until the next hourly instillation. For ulcus serpens, the application locally with a cotton-wool swab seems best, but it may probably need repetition.

As the result of experiments, which he began in 1907,[27] with the object of obtaining spectacles to protect the eyes of glass-workers from injurious rays and prevent "glass-makers' cataract," Sir William Crookes has succeeded in preparing, by the use of various metals, a glass which will cut off over 90 per cent. of heat rays and the whole of the invisible ultra-violet rays, and which is sufficiently free from tint to be capable of practical use. Testing with suitably screened, sensitive, photographic plates, he found that X-rays were not emitted by highly incandescent molten glass at a temperature of 1,000° to 1,500°, and that glass-makers' cataract must be ascribed rather to heat rays than to ultra-violet rays. It is interesting to note in this connection that the operatives are sometimes exposed to the radiation from as much as three or four hundred tons of molten glass, covering an area of some 82 square yards.

It must be remembered that rays having wave lengths of below λ7,230 are infra-red, those of the visible spectrum vary from λ7,230 to λ3,970, whilst those above λ3,970 are ultra-violet. Two specimens of the glass prepared are now upon the market, and are known as Crookes's glass No. 1 and No. 2. The No. 1, whilst being almost free from noticeable tint, transmits 99·5 per cent. of luminous rays, cuts off 37·1 per cent. of heat rays, and the ultra-violet limit is λ3,700. The No. 2 is more suitable for glare, having a moderate tint and transmitting 83·4 per cent. of luminous rays, cutting off 34·7 per cent. of heat rays, and possessing an ultra-violet limit of 3,600. Although the ideal glass, which should transmit all

the luminous rays and cut off all the invisible rays, has not yet been discovered, these two samples give all the luminosity and supply all the protection that is practically needed, and are proving of considerable service for many ordinary and special purposes.

The glass-workers do not appear to realize the risks from which their eyes can now be protected as a result of Crookes's researches, and, not appreciating the prevalence of cataract amongst them, they have complained that the glasses make their eyes feel hot, do not improve their condition as far as glare is concerned, and that they cannot work in them. Probably nothing will overcome their conservatism but compulsory legislation. As showing the prevalence of the disease, Dr. T. M. Legge,[28] of the Home Office, has reported that out of 513 glass blowers he found cortical cataract in the right eye in 64 cases, and in the left eye in 72 cases. Cridland has brought forward a case of cataract in a "puddler," and Golden has mentioned one in a "welder." Priestley-Smith has suggested an excellent and inclusive designation for all these cases, viz., "furnace-workers' cataract."

An interesting discussion upon the subject of workmen's compensation and eye injuries took place at the Oxford Ophthalmological Congress last July.[29] By the Workmen's Compensation Act, 1906, "If in any employment, personal injury by accident arising out of and in the course of the employment is caused to a workman his employer shall . . . be liable to pay compensation." The proof of negligence is no longer necessary, and the injured man is paid half of his wage up to the maximum of £1 per week during total incapacity, and when certified for light work he is compensated for the reduced wage which he earns by a further sum generally equal to half the reduction.

The total number of claims under the Act now number about half a million annually; the cost to the employer is from ½ per cent. to 1½ per cent. of the wages bill, according to the risk of the employment.

Malingering is greatly on the increase, and one speaker estimated that 16 per cent. of the ophthalmic cases, on which he had reported during the previous five years, had shown evidence of gross malingering. The weekly payment of compensation accounts for the increasing number of claims,

as well as for the length of time individuals absent themselves from work. The immediate improvement in wage-earning capacity after payment of a lump sum is often remarkable, for then, as has been remarked, "the lawyers cease from troubling and the workman is at rest." Looking at this subject from the ophthalmic point of view alone, employers and insurance companies would find it an economy and check on malingering if they would insist on workmen being medically examined before they are taken on. For instance, the existence of chronic dacryo-cystitis may lead to the pneumococcal infection of a minute corneal abrasion with consequent partial or complete loss of the eye, for which the employer would be held responsible; or a pre-existing and un-noted squint, with amblyopia in connection therewith, may enable a successful claim to be made for some trifling injury which has not in any way affected the individual's eyesight or capacity for work. After a trifling, superficial injury a worker may by some kind of irritation, keep up a chronic conjunctival congestion or inflammation, and, in spite of medical evidence, carry his case successfully through the County Court, and then sue later for a "declaration of liability."

As one contributor said, "A workman, claiming compensation can make the most exaggerated claim, can practise the most glaring malingering, be proved an arrant liar, and yet fear no punishment if his case is proved to be a bogus one." Great care should be taken by hospital medical officers in giving certificates in cases of injury, and nothing should be stated, but that the applicant is a patient at the hospital and unable to work, if that be so. The habit of giving a placebo merely to satisfy such a hospital patient should not be followed, for, to the legal mind, the giving of the most simple lotion implies that there must have been some pathological necessity for it.

The discussion elicited a general feeling that there has been, and still is, a tendency to over-estimate the disability resulting from the loss of one eye. Excluding seamen, engine-drivers, and ironworkers, most others can after a time perform their duties almost as well with one eye as with two. Cases of injury due to the loss of binocular vision are rare, whilst insurance companies do not object to insure one-eyed workmen. In reporting on cases of injury, the statements made by

the workman as to the accident and its effect in preventing him working should be clear and concise; the condition found on examination should be clearly described in as intelligible language as possible, and on the preceding data, an honest unbiassed opinion should be given of the extent of the disability with an estimate of its duration.

The surgeon should do his best to encourage the patient to return to some kind of work as soon as he is fit, for the longer the absence from work the greater the inclination to develop a loafing, lazy, neurasthenic, or even malingering habit.

It is impossible to go into all the details of the discussion, which is well worth reading in full.

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THE DUODENUM IN DIABETES MELLITUS.*

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[With Plates XLIII.–XLIV.]

It is usually considered that, in diabetes mellitus, the changes in the function of the pancreas form the basis of the greater part of the symptom-complex. The inception of the morbid process, however, lies behind this pancreatic landmark, and evidence is brought forward in the present paper to show that specific lesions are present in the duodenum, which probably precede the dissolution of the pancreas.

The vertical length of the duodenal shadow, measured orthodiagraphically after a bismuth meal, is less than $3\frac{1}{2}$ inches in healthy adults, being approximately equal to the length of two lumbar vertebræ with their intervening discs. Reference to the protocols appended will show that in nine consecutive patients with severe diabetes mellitus, the mean vertical length of the duodenum was $3\frac{1}{5}$ vertebræ, the extremes being 3 and $3\frac{1}{2}$. Considering adults only, the average length was $4\frac{4}{5}$ inches, and the extremes $4\frac{1}{2}$ and $5\frac{1}{2}$ inches respectively. These figures represent a very great enlargement of the organ; in fact, W. B.'s duodenum was twice as long as that of a healthy adult. Not only is this part of the alimentary canal elongated, but it is increased in calibre also, and on examination after death, the walls can be seen to share the same change, being thick and fleshy, and of a somewhat milky appearance. The same alterations in structure can be traced in the upper portions of the jejunum.

This enlargement is almost invariably associated with ileal or colonic stasis, and in some patients delay is so extreme, and the consequent modification of the lower bowel so advanced, that there can be no doubt but that alimentary stasis preceded the onset of diabetes; as, for example, in the case of X. N., whose duodenum showed strong antiperistaltic movements. The duodenal dilatation of such patients might reasonably be ascribed to the factors which

* From the Guy's Hospital Laboratories. The expenses of the research were defrayed by a grant from the British Medical Association.

Fig. 1.—*Large annular duodenum usually present in diabetes mellitus.* (P = *Pylorus.*)

Fig. 2.—*Duodenum from a patient with moderate intestinal stasis. Elongation and obstruction are not very great. Contrast with the duodenums in* Figs. 1 *and* 3.

Fig. 3.—*Typical V shaped obstructed duodenum from a patient with intestinal stasis.*

Fig. 4.—*Large distended duodenum in which enlargement is secondary to obstruction produced at the duodenojejunal flexure by operative interference.*

produce this abnormality in simple intestinal stasis. In the majority of cases, however, the increase in size of the upper part of the small intestine is the predominant change in the alimentary canal, while lower bowel delay and duodenal regurgitation, although present, are not sufficiently pronounced to account for the enlargement. Fæcal accumulation is evidently a common concomitant of diabetes mellitus, but not the sole determining factor although it may be a predisposing cause. That ileal stasis plays an important part in the disease is clearly shown by the following analysis, in which the patients are classified according to the severity of their acidosis.

Number of Cases.	*Acidosis.*	*Urine Reactions.*			*Ileal Stasis.**
		Ferric Chloride.	Legal's Reaction.	Rothera's Reaction.	
2 (2 and 8.)	Died in Coma	+	+	+	2+
5 (1, 3, 5, 6, 7.)	Severe	+	+	+	1+
2 (9 and 10.)	Moderate	−	+	+	¼+
2 (4 and 11.)	Slight	−	−	+	⅛+

The intensity of the disease is here seen to be directly proportional to the degree of ileal stasis, although there are isolated exceptions to this rule in young people, in whom the presence of stasis is more difficult to determine. Almost all diabetic patients excrete indoxyl, indolacetic acid, and parahydroxyphenylacetic acid in their urine, in varying proportions. In constipated subjects, these substances arise either directly or indirectly from the action of B. coli on tryptophane and tyrosin in the small intestines, and the amounts excreted serve as an index of the extent to which the ileum is infected with coliform organisms.[1] In diabetes mellitus, the excretion of these bodies does not bear any

* The following convention is made use of in measuring ileal stasis. A bismuth meal is given, and no further food until the stomach is empty. Failure of the bismuth to reach the cæcum in 4 hours and the presence of a little bismuth in the ileum after 8½ hours = ileal stasis (+) (value = ¼). A definite collection seen between 8½ and 9 hours = ileal stasis +. A definite collection seen between 9 and 24 hours = ileal stasis 2 +. A definite collection seen after 24 hours = ileal stasis 3 +.

obvious relationship to the severity of the disease, from which fact it may be inferred that the gravity of the prognosis in diabetics, with marked ileal delay, depends upon some condition other than the coincident infection of the small intestine with coliform organisms. It has been demonstrated by Sir Arbuthnot Lane,[2] and confirmed by other observers,[1 3] that stasis in the ileum impedes the passage of chyme through the duodenum by producing obstruction at the entrance to the jejunum. The very instructive work done in America by W. Seaman Bainbridge and A. J. Quimby[4] is of particular interest in connection with this point. Such stagnation would be detrimental to a duodenum already injured by disease, and affords a reasonable explanation of the adverse effect of ileal stasis in diabetes.

S. G., a feeble, sallow boy, aged 11 years, under the care of Sir Arbuthnot Lane, had lost weight and suffered from excessive thirst for three months. Defæcation was irregular, and his abdomen a little distended but he was free from any discomfort which could be referred directly to his alimentary canal. His teeth were good, his tongue clean, and his fauces healthy. A bismuth meal passed through the pylorus in about 4½ hours. It was delayed in the duodenum which was elongated and distended, the vertical limb measuring 3½ inches or 3 vertebræ. The ileum was not completely emptied until the 11th hour, whereas a normal ileum would have been empty before the 8th hour. Bismuth began to enter the cæcum in 4½ hours, reached the hepatic flexure in 8½ hours, and the pelvic colon in 30 hours. It was partially evacuated at the 32nd hour, but much remained in the pelvic colon until after the 76th hour. A little stasis was thus observed in the stomach and duodenum, and considerable stasis in the ileum, colon, and rectum. The duodenum and pelvic colon were greatly increased in size. His Wassermann reaction was negative. He excreted about 240 grammes of sugar daily, and his urine always gave the ferric chloride reaction for diacetic acid. Sir Arbuthnot Lane removed the colon, and withdrew some of the contents of the enlarged duodenum by means of a syringe. From this fluid an exceedingly abundant growth of streptococcus brevis was obtained.

The following table of observations on duodenal contents, removed at laparotomy in a variety of conditions, demonstrates

the unique character of this infection :—

Number of Cases.	Nature of Case.	Number of *colonies of streptococcus brevis* grown on two nutrose agar plates from five platinum loops full of duodenal chyme.
2	Simple chronic intestinal stasis - - -	0
1	Intestinal stasis with arterial hypotension -	0
1	,, ,, ,, very distended duodenum	0
1	,, ,, ,, intense anæmia and pigmentation.	0
2	,, ,, ,, incipient insanity - -	0
1	,, ,, ,, chronic duodenal ulcer and hyperchlorhydria.	0
1	,, ,, ,, chronic gastric ulcer -	0
1	,, ,, ,, appendix controlling the ileum.	0
1	Tuberculous enteritis with appendix controlling the ileum.	0
1	Rheumatoid arthritis - - - - - -	0
1	,, ,, with endemic goitre -	0
1	,, ,, - - - - - -	140
1	Raynaud's disease - - - - - - -	2
	TOTAL 15 CASES - - - - - -	142
1	DIABETES - - - - - - -	2,000

Before giving details of the cases I will recapitulate the facts substantiated in this paper—

1. Diabetes mellitus is associated with great enlargement of the duodenum which cannot be accounted for wholly by coincident intestinal stasis.

2. A profuse growth of streptococcus brevis was obtained from the duodenum of a boy with severe diabetes mellitus. Such an infection has not been found in any other condition.

3. Ileal stasis is usually present in diabetes mellitus, and, in proportion to its severity, affects the prognosis adversely.

4. The urine of patients suffering from diabetes mellitus usually contains one or more products of the action of B. coli on tryptophane and tyrosin.

The suggested explanation of these phenomena is that chronic duodenitis is the determining factor in the production of diabetes mellitus, and that ileal delay increases the severity of the disease by causing stagnation in the duodenum.

Name. Age.	Diabetic History and General Condition.	Glycosuria.	Acid Excretion.	Alimentary History.		Abdominal Signs.	Indoxyl (I.) Indolacetic Acid (I. A.) Parahydroxy Phenylacetic Acid (P.) in Urine.	Bismuth and X-ray Examination.	Remarks.
				Stomach.	Intestines.				
1. M. T. 8	2 weeks' thirst and loss of weight. Nutrition good.	8 per cent. 168 grms. P.D.	$FeCl_3$ +	Normal	Bowels irregular.	None	I. – I.A. – P. –	Stomach :— Normal. Empty in 4 hours. DUODENUM :— Bismuth passed slowly. Duo. 2 = 3″ or 3 vertebræ. Ileum :— Empty in 8 hours. Colon :— Sigmoid long and transverse, rather low. Bismuth reached cæcum in 4 hours, extended from hepatic flexure to sigmoid after 32 hours, remained unaltered after 48 hours.	
2. S. G. 11	3 months' thirst and loss of weight. Thin and sallow.	7 per cent. 240 grms. P.D.	$FeCl_3$ +	Normal	Bowels irregular.	A little general distention.	I. – I.A. + P. –	Stomach : Normal. Empty in 4½ hours. DUODENUM :— Bismuth distended and passed slowly. Duo. 2 = 3½″ or 3 vertebræ. Ileum :— Contained bismuth after 10½ hours.	Died in coma a few weeks after these observations had been made.

								Colon :— Sigmoid long. Bismuth entered cæcum in 4½ hours, reached hepatic flexure in 8 hours and the pelvic colon in 30 hours. It was partially evacuated after 32 hours. Much remained in pelvic colon after 76 hours.
3. A.W. 16	7 months' thirst, hunger and wasting. Nutrition moderate.	8 per cent. 192 grms. P.D.	$FeCl_3$ + Trace of albumen in urine.	Normal	Normal	None	?	Stomach :— Normal. Empty in 4 hours. DUODENUM :— Bismuth passed slowly. Duo. 2 = 4½″ or 3 vertebræ. Ileum :— Most bismuth left the ileum in 8 hours, but traces remained for 12½ hours Colon :— Bismuth reached hepatic flexure in 5½ hours, the descending colon in 10 hours, the rectum in 12½ hours. Some was evacuated after 24 hours. Much remained in the sigmoid and rectum until a second evacuation at 47th hour.
4. F. L. 28	8 years' thirst and loss of weight. Nutrition moderate.	6 per cent. 145 grms. P.D. (Restricted diet.) 8 per cent. 165 grms. P.D. (Unrestricted diet.)	$FeCl_3$ − Legal (+) Rothera + $FeCl_3$ − Legal − Rothera −	Normal	Life-long constipation.	Last coil of ileum, tender.	I + I.A. + P + (Faintly)	Stomach :— Normal. Empty in 4 hours. DUODENUM :— Strong regurgitation from the 3rd to the 2nd part. Distention and elongation. Duo. 2 = 5″ or 3¼ vertebræ.

Name. Age.	Diabetic History and General Condition.	Glycosuria.	Acid Excretion.	Alimentary History. Stomach.	Alimentary History. Intestines.	Abdominal Signs.	Indoxyl (I.) Indolacetic Acid (I. A.) Parahydroxy Phenylacetic Acid (P.) in Urine.	Bismuth and X-ray Examination.	Remarks.
4. F. L. 28 *cont.*								Ileum :— Thick and distended. Empty in 8 hours. Colon :— Bismuth entered the cæcum after the 4th hour, reached the ascending colon by the 6th hour, the splenic flexure at the 8th hour and the pelvic colon at the 28th hour. The transverse colon was a little dropped.	
5. A. B. 33	1 month of increasing weakness.	6 per cent. 360 grms. P.D.	$FeCl_3$ + Traces of albumen.	Occasional flatulence.	Normal	None	I + I.A. + (Faintly) P −	Stomach :— Normal. Empty in 5 hours. DUODENUM :— Bismuth passed very slowly, and distended. Duo. 2 — 5″ or 3¾ vertebræ. Ileum :— Traces of bismuth present after 10 hours. Colon :— Bismuth reached the splenic flexure in 5 hours, occupied the transverse and pelvic	

								colons after 23 hours and the pelvic colon and rectum after 48 hours.
6. J. M. 40	4 months' polyuria and loss of weight.	7 per cent. 210 grms. P.D.	$FeCl_3$ + (Faintly).	Normal	Somewhat constipated.	None	I. − I.A. + P. + (Faintly)	Stomach :— Normal. Empty in 4 hours. DUODENUM :— Duo. 2 = $4\frac{1}{2}$″ or 3 vertebræ. Ileum :— Contained much bismuth after 9 hours. Colon :— Bismuth entered the cæcum after the 4th hour and reached the sigmoid in 28 hours. The transverse colon was a little dropped.
7. W. F. 43	2 months' hunger, thirst and loss of weight. Nutrition poor.	6 per cent. 150 grms. P.D.	$FeCl_3$ +	Normal	Normal	Slight tenderness over the last coil of ileum.	I. + I.A. + P. −	Stomach :— Normal. Empty in $4\frac{1}{2}$ hours. DUODENUM :— Bismuth passed slowly and distended. No regurgitation. Duo. 2 = $4\frac{1}{2}$″ or 3 vertebræ. Ileum :— Thick. Empty in $8\frac{1}{2}$ hours. Colon :— Bismuth entered after 4th hour, reached the transverse colon in 8 hours, the splenic flexure in 24 hours, and the rectum in 48 hours. A little was evacuated at the 44th hour. The transverse colon was a little dropped.

Name. Age.	Diabetic History and General Condition.	Glycosuria.	Acid Excretion.	Alimentary History. Stomach.	Alimentary History. Intestines.	Abdominal Signs.	Indoxyl (I.) Indolacetic Acid (I. A.) Parahydroxy Phenylacetic Acid (P.) in Urine.	Bismuth and X-ray Examination.	Remarks.
8. X. N. 47	6 months' thirst, polyuria and wasting. Emaciated.	5 per cent. 143 grms. P.D.	$FeCl_3$ + A trace of albumen.	Loss of appetite.	Alternate constipation and diarrhœa for many years. Severe constipation for 1 year.	Last coil of ileum thick and tender. Colon palpable from cæcum to sigmoid.	?	Stomach :— Large and active. A little pyloric spasm. Not empty in 9 hours. DUODENUM :— Greatly dilated with strong regurgitation from the 3rd to the 2nd parts. Only traces of bismuth reached the jejunum during the first 15 minutes. Ileum :— Contained much bismuth after 6 hours and some after 23 hours. The terminal coil was thick and bound down. Colon :— Bismuth entered the cæcum at the 7th hour, reached the hepatic flexure after 23 hours, the middle of the transverse after 30 hours, and the splenic flexure after 95 hours. The transverse colon was very long and tortuous.	Food was given before the bismuth had left the stomach. Died in coma about a week after these observations had been made.

9. W. B. 49	8 years' slowly increasing thirst and loss of weight. Nutrition good.	8 per cent. 215 grms. P.D. On a restricted diet, 40 grms. P.D.	Legal – Rothera + (Faintly). $FeCl_3$ – Legal + Rothera + (Strongly).	None	Constipation for 1 year.	None	I. + I.A. + P. +	Stomach :— Normal. Empty in 4 hours. DUODENUM :— Bismuth passed through slowly and did not regurgitate. The organ was greatly distended and elongated. Duo. 2 – $5\frac{1}{2}$" or $3\frac{1}{2}$ vertebræ. Ileum :— Empty at the 9th hour. Colon :— Bismuth began to enter the cæcum after 4 hours, reached the transverse colon in 9 hours, was all in the descending colon in 25 hours, and was all evacuated at the 44th hour.
10. C. P. 52	18 months' thirst, polyuria and loss of weight.	12 per cent. 175 grms. P.D. The sugar disappeared from the urine after 3 weeks' treatment on a carbohydrate free diet. One slice of toast caused it to reappear.	$FeCl_3$ – Legal +	None	Constipated for several years.	Last coil of ileum, tender.	?	Ileum :— A little bismuth present after 8 hours. Colon :— Bismuth reached the transverse colon by the 8th hour. A little was evacuated at the 25th hour. Most of the bismuth extended from the cæcum to sigmoid after 32 hours. The transverse colon had dropped to the pelvic brim.

Name. Age.	Diabetic. History and General Condition.	Glycosuria.	Acid Excretion.	Alimentary History. Stomach.	Alimentary History. Intestines.	Abdominal Signs.	Indoxyl (I.) Indolacetic Acid (I. A.) Parahydroxy Phenylacetic Acid (P.) in Urine.	Bismuth and X-ray Examination.	Remarks.
11. E. S. 65	7 years' thirst and excessive appetite with polyuria; gangrene of the left foot. Nutrition good.	7 per cent. 130 gms. P.D.	$FeCl_3$ – Legal – Rothera + (Faintly).	Normal	Normal	None	?	Stomach :— Normal. Empty in less than $5\frac{1}{2}$ hours. DUODENUM :— Distended. No regurgitation. Duo. 2 – $4\frac{1}{2}$'' or 3 vertebræ. Ileum :— Empty after 8 hours. Colon :— Bismuth reached the splenic flexure in $5\frac{1}{2}$ hours. Some was evacuated after 26 hours. Much remained in the rectum and sigmoid at the 32nd hour.	

For comparison with the X-ray examinations detailed in the foregoing protocols, I quote Dr. A. C. Jordan's description of the normal alimentary tract from his article in Sir Arbuthnot Lane's book on *The Operative Treatment of Chronic Intestinal Stasis.* "In a normal case the bismuth passes rapidly through the œsophagus into the stomach, when regular peristaltic waves are seen, and small portions of bismuth may enter the duodenum. The result of the introduction of bismuth is that in the erect posture, the greater curvature falls about one inch below the level of the umbilicus. Examining the patient on the couch, regular peristaltic waves move along both curvatures to the pylorus and bismuth enters the duodenum and passes through the four parts of the duodenum as the result of a normal duodenal peristaltic wave, and enters the jejunum. The duodenojejunal junction is rounded, offering no obstruction to the course of the bismuth. The second part of the duodenum measures $2\frac{3}{4}$ to $3\frac{1}{4}$ inches. It is usually impossible to obtain a skiagram of the normal duodenum for with an ordinary 'time' exposure the bismuth may be seen to leave the duodenum after a few seconds. If an instantaneous method be used, but a portion of the (normal) duodenum is shown, for only a part of it contains bismuth at any particular moment. *By the end of two or three hours,* the whole of the bismuth has left the stomach, being seen widely scattered through the small intestine, but especially in the lower coils of the ileum above the pelvic brim. *After three-and-a-half to four hours,* bismuth has begun to enter the cæcum. *After five or six hours,* there is no longer any bismuth in the small intestine, the whole of it occupying the cæcum and ascending colon. *At the end of eight to twelve hours,* some bismuth has reached the splenic flexure. *After twenty-four hours,* the bismuth is distributed through all parts of the large intestine, some having reached the rectum or been evacuated. *At the end of forty-eight hours,* the whole of the bismuth has been evacuated."

I wish to thank the staff of Guy's Hospital for affording me opportunities for making these observations on patients under their care.

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THE TREATMENT OF SOME SEPTICÆMIAS BY VACCINES.*

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IN this paper, I propose to consider, shortly, the treatment by vaccines of some generalized infections or septicæmias, as distinct from localized infections. I have chosen this class of case, for I think the value of vaccines is not as yet so generally recognized in these cases as in well-localized infections, and also because I have had the opportunity of dealing with some hundreds, many more in fact than most men fortunately come across in a lifetime.

In the early days of inoculation treatment, it was considered to be a method applicable to local infections only, and infections which were generalized, *i.e.*, septicæmias, were considered to be outside the range of such treatment. Later, however, these views were modified, and now are entirely altered. This alteration has, I think, taken place owing to the fact that we have a better appreciation of the conditions existing in a septicæmia.

The concept of a septicæmia, which used frequently to be held, was a condition in which the infecting organism had gained entrance to the blood stream and was circulating and multiplying there, the primary focus through which entrance had been gained having become of secondary importance. This concept had, as its origin, the purely artificial laboratory experiments of inoculating a highly susceptible animal with an organism of great virulence, which did, no doubt, circulate and multiply in the blood stream, and produced death in 24–48 hours. This, however, is not a picture which is seen in practical medicine in this country. The cases of septicæmia which we see are cases of local infection, in which the tissues have not responded sufficiently to build up a barrier to shut it off from the general circulation; consequently, some of the bacteria are carried away into the blood stream, and a

* Based on a Paper read at the Hunterian Society.

positive blood culture may be obtained. There is, however, little evidence that, during life, these bacteria are able to multiply there, or even that they can retain their vitality there for any great length of time. On the contrary, there is much evidence against this; *e.g.*, if we withdraw 10 cc. of blood from the vein in a case of septicæmia, and put 2 cc. in a sterile test tube, 2 cc. in 10 cc. of broth, 2 cc. in 20 cc. of broth, 2 cc. in 50 cc. of broth, etc., we shall, after incubation, often obtain no growth in the undiluted or slightly diluted samples but abundant growth in the highly diluted samples. The interpretation of this is, that the fresh blood is not a suitable medium for growth, being even in a case of septicæmia relatively powerful in antibodies, and it is not until these antibodies have been diluted with the broth that the bacteria have been able to grow.

Again, we may take a blood sample from the same patient on several occasions, and obtain a growth at one time, but fail entirely only a few hours later. This is usually when the first has been taken near to the occurrence of a rigor.

These questions then arise: Why do the local tissues respond insufficiently to the stimulus of the primary infection? Why, if the bacteria are present in the blood stream, is the stimulus still insufficient?

The response of the local tissues depends on the stimulus being adequate without being excessive. If the stimulus is too great, either owing to excessive dosage or excessive virulence, the local infected tissues are paralysed and killed, and are unable to respond; secondly, it is not the blood stream that we wish to stimulate but rather the fixed cells, for much evidence goes to indicate that it is there that we must look for the production of antibodies.

On these grounds, therefore, inoculation treatment was extended to generalized infections, and the results have justified this extension.

Coming then to a consideration of these cases in more detail, I propose to divide them up for convenience of discussion into four groups. These groups are of course to some extent artificial and arbitrary, but will be useful in tabulating our ideas.

Firstly, a group, examples of which all physicians will

come across from time to time, namely, progressive endocarditis. This condition, as septicæmias go, is a slow process, and usually between the diagnosis and the fatal termination of the disease there is ample time for adequate bacteriological examination, etc. This is due to the fact that the infecting organism is one of comparatively low virulence, and one which probably only produces a septicæmia owing to the site of infection being on the valve, and therefore impossible to localize. The commonest organism to find in these cases is a short-chained, non-hæmolytic streptococcus, similar to the streptococcus common in the mouth, and termed S. salivarius.

A certain number of cases of progressive endocarditis, which have been treated with autogenous vaccines, have been published, and a few cures claimed. In the successful cases, however, it must be remembered that the diagnosis rested on a balance of probabilities, and that the absolute diagnosis of the post-mortem room has necessarily been absent.

Personally, I have now treated 25 cases, but I cannot say that I have ever seen an undoubted case permanently cured. I have seen cases benefited. The temperature will steady under inoculation treatment from a maximum of 103° F. to 100° F. or 101° F., but the blood culture will not remain negative for more than short periods. I have seen such cases improve sufficiently to leave hospital after many months, but I would not say that they were cured.

From a consideration of these cases in the light of post-mortem room findings, I think it is difficult to see how a cure can be brought about, unless the diagnosis can be made in the very earliest stage of endocardial infection ; at such a stage, in fact, that, except for the subsequent progressive character of the disease, there could be no certainty about its accuracy. The site of infection here is a valve, usually previously damaged. A streptococcus gains entrance to the blood stream probably through the tonsils. In a normal person, this would very soon be dealt with by the normal defences, and would find no foothold. A damaged valve, however, is a weak spot, and here the coccus may settle. A fibrinous vegetation forms, and in this the coccus can grow. This vegetation is not vascularized, and, consequently, it is not possible, even though the blood contains

antibodies, for the bacteria in its substance to be destroyed. The vegetation hanging in the blood current is more or less continually throwing off bacteria and emboli. I look upon progressive endocarditis, therefore, unless it can be diagnosed extremely early in the course of the infection, as one of the limitations of vaccine therapy.

Secondly, I wish to discuss a condition which probably many of us never see in practice, namely, puerperal septicæmia. There are in England and Wales about 1,300 cases notified per annum, with a mortality of about 60 per cent. In a series of over 200 cases, the severity of which is above rather than below the average, we have had a mortality of under 40 per cent. These cases, unlike the cases of endocarditis, are very virulent and acute infections, and time, therefore, is of very great importance. The question consequently arises: Can we use a stock vaccine, which can be given without loss of time?

The first essential to specific therapy is specific diagnosis. Puerperal septicæmia is caused by a variety of different organisms, and, consequently, it is unwise to rely entirely on a stock vaccine. I have now isolated and examined nearly 150 strains of bacteria from these cases, and I find that the streptococcus pyogenes is the infecting organism in over 80 per cent. of cases, and, therefore, in any case of great urgency I advise that a dose of vaccine from a known reliable strain of streptococcus, derived from a puerperal case, should be given, and at the same time cultures should be taken and an autogenous vaccine prepared with all possible speed. Cultures should be taken both from the blood and from the primary focus of infection. This is, in almost all cases, the placental site, although occasionally it is lacerations about the perineum or vagina.

I lay stress on the importance of cultures from the uterus, for by this means, in the majority of cases, an autogenous vaccine can be ready in 24 hours.

In a paper on this subject, which I read before the Obstetrical Section of the Royal Society of Medicine in 1912, I pointed out that, provided an efficient technique was carefully followed, with some experience one could obtain a *pure culture* of the infecting organism direct from the uterus in 77 per cent.

of cases. I am now able to raise that percentage to about 90 per cent. This is of extreme importance, for it avoids the time spent over plating out and isolating various organisms, and then having to decide which is the cause of the trouble. Needless to say, the mere passage of a wire or swab into the cervix is absolutely useless, for it will never produce a pure culture.

With regard to dosage in these cases, I advise comparatively small doses, 2–5 million cocci, repeated according to clinical indications, usually after an interval of 24–48 hours. It is essential in these cases that a 4-hourly chart, at least, of the temperature and pulse should be kept accurately, for the ordinary morning and evening chart alone is often very misleading.

If the case responds, the temperature may come down by crisis and not rise again above 100° F., or there may be a fall of 1° F. on the mean of the six 4-hourly temperatures after each injection. A corresponding fall in the pulse rate should occur too. In fact, in all cases of septicæmia the character and rate of the pulse is of very great prognostic value.

If the temperature steadies to a maximum of 101° F. or 102° F. and fails to come lower, it usually indicates that peri- or para-metric inflammation has occurred, and that the infection has ceased to be generalized and is now localized. The prognosis is then correspondingly better, but the convalescence may be prolonged.

If rigors are a prominent feature and continue in spite of inoculations, the probability is that there are thrombosed septic veins throwing off bacteria and emboli into the blood stream, which from their position cannot get localized. The prognosis then is bad. Repeated rigors, however, in an untreated case may respond to treatment in a very marked way. I have seen a patient, who had been having rigors at least once a day for six weeks, cease having rigors after the first dose of vaccine, make a complete recovery, and become the mother of more children.

In my third group of septicæmias, I propose to discuss very briefly some cases which come more often under the general practitioner or the surgeon. They are often of very great virulence, and frequently originate in a most trivial wound.

Such cases are seen from time to time amongst medical men and nurses following on accidental wounds, punctured or incised, during operations on, or dressing of, infected cases. Needless to say, such injuries must always be taken seriously from the outset, remembering that direct passage of an organism from one susceptible subject to another is the finest way to exalt its virulence; remembering, too, how many of our profession have lost their lives through such seemingly trivial injuries. Similar cases occur frequently amongst the laity, when it is often impossible to trace the source of infection.

An insignificant wound or mere scratch, a blistered foot or an in-growing nail, may have been present for days and be well on the way to complete healing, when from some source unknown it becomes infected with a virulent organism. In the course of a few hours, a strong vigorous person is reduced to one seriously ill, with a temperature of perhaps 104° F., rigors, and spreading lymphangitis showing in bright red streaks up to the groin or axilla, or acute enlargement and tenderness of the epitrochlear and axillary glands. Such cases as these, needless to say, require immediate treatment. Active measures to ensure efficient drainage of the primary focus must be carried out at once, but beyond that, active surgical measures lend little aid in localizing the process. Excision of the acutely-inflamed glands and multiple incisions into cellular tissues are sometimes done, but these appear to me to be pathologically unsound, and the results are not encouraging.

The condition is essentially one of excessive virulence of infection, as compared with the resistance of the host. If we can by artificial means help the patient to a rapid increase in specific resistance, this will hold out the best hope of checking the process. An anti-serum in such cases should be of great value in theory. In practice, however, antistreptococcus serum has been a very great disappointment. There appears to be little evidence that many of these sera on the market contain any antibodies at all.

On the other hand, active immunization by means of vaccines, provided it is undertaken promptly, gives hope of good results in many cases.

As one has already indicated, specific therapy requires

specific diagnosis. The question therefore arises: Can we be reasonably certain what the infection is without waiting for a complete bacteriological examination?

For the most part, these cases, in which there is rapidly spreading lymphangitis, etc., are due to the streptococcus pyogenes, and therefore, I think, a small dose of a reliable strain of this organism should be given at once. At the same time, it must be remembered that a certain number of such cases are due to the staphylococcus aureus, so that, if there is doubt, it may be wise to begin with both, until a definite diagnosis is made. The staphylococcal cases more readily subside on adequate drainage of the primary focus, and usually do not spread so rapidly. More rarely, the infecting organism may be a pneumococcus or some other organism. By the end of from 24 to 48 hours, it should usually be possible to have an autogenous vaccine ready.

The following cases illustrate this group well:—

1. A man received a slight abrasion on the knuckle of his forefinger. Eight days after, this was covered by a firm scab, and he was perfectly fit and well when he retired for the night. Early next morning, he woke up with pain and throbbing in the finger and up the arm. He came up to hospital with a temperature of 102° F., shivers, and feeling very ill. The knuckle was acutely inflamed, and there was a bright red streak running up the line of the lymphatics as far as the axilla. Such a case one has learnt to look upon as of considerable gravity. I saw him at 11 a.m. On raising the scab there was no pus, but on squeezing out a minute trace of serum one found swarms of streptococci. I therefore gave him an injection of streptococcus vaccine at once. This preliminary examination was confirmed by obtaining pure cultures of streptococcus in 24 hours, from which an autogenous vaccine was made. The lymphangitis, after the first injection, spread no further, and at once commenced to be well localized. After six days, there was a small soft area from which ½ oz. of pus was obtained. The temperature improved after the first injection, a slight evening rise continuing until the acute lymphatic inflammation had subsided.

2. A young man had had some slight suppuration around a finger nail for some days. From this spreading lymphangitis commenced, and the epitrochlear and axillary glands became acutely inflamed. The axillary glands were dissected out, and on examination were found to be swarming with streptococci and to contain no pus. After the operation, the temperature remained above 103° F., and there appeared to be no indication of localization. An autogenous vaccine was therefore given, and within 48 hours the temperature fell to 99° F., and recovery was rapid and without any complication.

This group of cases, I would urge therefore, are such that,

unless they rapidly respond to measures directed to the primary local lesion, they should be given the benefit of vaccine treatment, for I am convinced that a delay of 24 hours may, in the more virulent infections, make the difference between life and death.

Lastly, a very few words about a class of case, fortunately not so common now as previously, which is seen chiefly by the surgeon, namely, post-operative septicæmia or pyæmia.

The true post-operative septicæmia with spreading cellulitis, etc., is now fortunately practically extinct. There are, however, and will continue to be a certain number of cases of septicæmia or pyæmia (no absolute distinction being possible) following after such operations as that for a gangrenous appendix or middle-ear disease with lateral sinus thrombosis or other operations, which from their nature are not what are called "clean" operations. These cases are usually characterized by rigors and the occurrence of pyæmic abscesses, due to the separation of septic thrombi.

The difficulty of dealing with these cases is the same as in similar cases of puerperal origin, namely, the root of the trouble is the presence of thrombosed veins which are infected. In my experience, the infecting organism in these cases, as determined by blood culture, is most commonly a streptococcus.

The treatment of these cases with vaccines is always worth trying, for many will at once cease having rigors, and make good and speedy recoveries. In particular, one has had very striking success in cases of septicæmia persisting for a week or more after the operation for acute mastoid and lateral sinus thrombosis, as well as in some cases of pyæmia following on acute abdominal operations, in which a marked feature had been the occurrence of numerous rigors and metastatic abscesses. There will, however, always be a percentage of cases, in which there are septic thrombi to such an extent or so placed that, by no active or passive process of immunization, can we bring about a cure.

RECENT WORK ON CLINICAL PATHOLOGY.

By W. D'ESTE EMERY, M.D., B.Sc., etc.

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CEREBRO-SPINAL FLUID.

The cerebro-spinal fluid is of special interest and importance to clinical pathologists, and many papers and articles dealing with it have appeared recently. Of these some of the most important are contained in a special number of the *Journal of Medical Research* (September, 1914).

Weed deals specially with the secretion, and, in fuller detail, with the paths of escape of the fluid. His papers are remarkable in the new and ingenious methods he has applied to these old and well discussed problems. In experimenting on the formation of the fluid, he introduced a cannula through the aqueduct of Sylvius into the third ventricle, taking care to use a catheter of such a size that the resistance to the flow of fluid through its lumen was just sufficient to keep the pressure in the cerebral ventricles normal throughout the experiment. In this way, he obtained cerebro-spinal fluid, which is secreted by the choroid plexuses alone, without admixture with the products of the perivascular system; moreover, the actions of drugs, etc. on the choroid plexus could be studied in a simple manner. The results are promised in a future communication.

The possibility that a little of the fluid may be secreted by the ependymal cells lining the ventricles, cannot be excluded. The only way in which this could be proved, is by finding histological changes in the cells in various stages of activity, and this Weed has not been able to do at present; in any case, the amount secreted must be very small. With regard to the second possible origin, suggested by Spina and others, Weed is of opinion that part of the cerebro-spinal fluid is formed in the so-called perivascular lymphatics as well, and represents the waste products of nerve-cell activity; the term "lymphatic," is unsuitable,

for the fluid contained in them is different from true lymph in every way.

Weed's observations on the escape of the fluid are more interesting and original. He reviews all older theories—Key and Retzius's view, that the escape is by means of the Paccionian bodies, is now known to be inaccurate, if only for the reason that they are often absent in young children, and always in anthropoid apes. Mott suggested that the absorption takes place in the substance of the brain itself, the watery part being taken into the capillaries by a process of diffusion and osmosis, salts and sugar passing in the reverse direction into the cerebro-spinal fluid. Leonard Hill showed that coloured substances injected into the cerebro-spinal fluid pass quite quickly into the venous sinuses, and Ziegler found that potassium ferrocyanide could be detected in ten seconds in the veins, but not in the lymph channels until half an hour after injection. Cathelin and others, however, thought that the main avenues of escape are the perivascular and perineural sheaths.

Weed's own researches were carried out by an ingenious method, to which apparently no theoretical objection can be raised. In brief, he injected an isotonic solution of potassium ferrocyanide and iron ammonium citrate in equal amounts into the subarachnoid space, and after the injection killed the animal and hardened its head with the brain *in situ* with a solution of formalin containing one per cent. of hydrochloric acid. This precipitated the ferrocyanide, in the form of Prussian blue, wherever the injection had penetrated. The solution is non-toxic, and care was taken to inject the fluid at low pressures, except in a few cases for particular purposes. After fixation, serial sections were cut and examined, and the distribution of the Prussian blue carefully studied.

The naked eye findings are :—The filling of the diploetic vessels with a blue deposit, the pale tinting of the dura, the marked outlining of the arachnoid channels, the perineural injection of the cranial nerves, the colouring of the cervical nodes and lymph channels, the bluish deposit in the nasal mucosa (of special interest in view of the occasional escape of the cerebro-spinal fluid from the nose), and the lining

walls of the cranial air cells. No deposit at all occurs in the subdural space, nor, except when the injection has been carried out under high pressure, in the cerebral veins. How, then does the fluid escape? According to Weed, the chief method is by a process of filtration through the arachnoidal villi into the great sinuses: there is, too, a certain amount of drainage by the lymphatic system, but this is quite unimportant except in the case of the spinal subarachnoid space.

He describes a villus as a voluminous, delicate, and lace-like sleeve, through the axis of which there is usually a cerebral vein passing to the dural channel. It is a delicate, web-like structure of interlacing cords, continuing the outer arachnoid membrane into the dural walls. It is covered by a cellular cap of mesothelial cells. It is through such structures as this that the fluid escapes, mainly by filtration, but perhaps also partly as well by osmosis and diffusion, into the sinuses, and hence into the diplœtic vessels. The whole paper is of great interest, and it is impossible to present an adequate summary here.

COLLOIDAL GOLD TEST FOR CEREBRO-SPINAL SYPHILIS.

This method was suggested by Lange[1] in 1912, and has recently attracted a considerable amount of attraction. The technique is fully described by Kaplan and McClellan.[2] The reagent is prepared in a scrupulously clean flask in which 500 c.c. of doubly distilled water are placed; this must not have come in contact with any rubber stopper or connection. To this 5 c.c. of a 2 per cent. potassium carbonate and 5 c.c. of a 1 per cent. solution of gold chloride are added, the fluid being gently heated. The heating is continued, and when the first bubbles appear, 5 c.c. of a ·75 solution of formalin are added, the flask being constantly shaken. An absolutely transparent solution of a deep, port-wine colour is formed.

The test is carried out as follows. Into the first of a series of carefully cleaned and sterilized test tubes, 1·8 c.c. of a fresh ·4 solution in sodium chloride is placed, and nine others receive 1 c.c. each. ·2 c.c. of the cerebro-spinal fluid, which must be clean, fresh, free from blood and iron rust, is added and stirred in, giving a 1 in 10 solution. Of this, 1 c.c. is added to the second tube, and stirred in, and the process

repeated with the remaining tubes, which thus contains ascending dilutions of the cerebro-spinal fluid up to 1 in 5,120 in the last tube. 5 c.c. of the reagent chloride, are added to each tube and thoroughly mixed by shaking. The reaction takes place quickly, but Kaplan and McClelland allow the tubes to stand all night, and read off the results next day.

The change consists in a complete or partial precipitation of the gold, leaving a colourless or partially coloured fluid. It is recorded in the form of a table, in which 5 stands for a perfectly clear and colourless fluid, 4 for a faint blue, 3 for a deeper blue, 2 for a reddish blue, 1 for a red but slightly different from the original fluid, whilst 0 indicates no change. A reaction is considered as positive, when there are three or more precipitations. Thus:—

GOLD CURVE.

Spastic paraplegia -	1 0 0 0 0 0 0 0 0 0 (negative reaction).
General paralysis - -	5 5 5 4 2 2 1 1 0 0 (positive reaction).

According to most workers the reaction is a general one, and can be obtained in all cases of syphilis of the central nervous system. The authors quoted deny this, and find marked and typical curves only in cases of general paralysis and tabo-paresis. They got a curve, but often not a characteristic one, in most cases of cerebro-spinal syphilis, whilst in tabes it was present only in low dilutions, if at all.

THE "NEWER BACTERIOLOGY" OF INFECTIONS.

Much attention has recently been paid to the question of so-called focal infection by the Chicago school (Billings, Rosenow, Davis, Jackson), which has had the advantage of having clinicians and pathologists engaging in team work. The results already obtained have been of considerable value, especially in connection with the pathology and treatment of rheumatism. We have here to outline the methods which have been introduced by Rosenow to secure cultures from the blood when ordinary methods fail, and also from solid tissues —a hitherto greatly neglected branch of pathology. It is by the application of his technique that he has isolated a diph-

theroid bacillus from all of over 40 cases of Hodgkin's disease, a diplococcus from the lymph glands in each of 7 cases of erythema nodosum, an anaerobic Gram-positive diplobacillus in 25 out of 32 cases of goitre, etc. The exact significance of these findings, which have been corroborated in some cases by other workers, is yet to seek, but their interest and importance is undeniable.

For blood cultures, Rosenow collects 15 to 30 c.c. of blood in the usual way, and adds it to 2 per cent. sodium citrate in saline solution, 5 c.c. of blood to 1 c.c. of solution. Some of this is planted out at once, and the rest is treated so as to get rid of the hæmoglobin, which, according to him, is adverse to the growth of streptococci. This is accomplished by adding one part of citrated blood to 10 parts of distilled water, and centrifugalizing; the two portions are planted out separately. The cultures are made in deep tubes of agar, ascitic agar, or serum agar, and, unless a considerable amount of living material is added, a piece of sterile guinea pig or rabbit tissue is placed at the bottom of the tube. In this way, Rosenow secures all gradations between absolute anaërobicity at the bottom of the tube and complete aërobiosis at the top. This is of importance, for some organisms will only grow in a particular concentration of oxygen. In some cases, he secures a gradation of acidity as well, by superimposing a plus one agar on a minus one, or *vice versâ*.

Tissues are excised with strict aseptic precautions, dipped into hot water or passed through a Bunsen flame, and rapidly cooled in sterile saline. They are then minced or crushed in a special "tissue crusher" which is contained in a large sterile tin-can provided with a mica window. At one end there is an indiarubber glove, which is tied on to a flange. The whole apparatus is sterilized by dry air, and the process of grinding and emulsifying the tissue is carried out by means of the hand inserted through the glove, so that the exposure of the material to the unsterilized air is reduced to a minimum. Rosenow's method appears to be simple and ingenious, and constitutes a decided addition to our technique.

THE ABDERHALDEN TEST FOR PREGNANCY.

This has continued to attract considerable attention during

the past year, and it is not unfair to say that opinion seems to be turning definitely against its value, and against the correctness of the theory on which it is based. The technique is so difficult and so fraught with errors, that experimenters obtaining incorrect results at first were inclined to attribute them to experimental errors. But now workers who have studied the technique with great care, are coming forward and denying the value of the method *in toto*, and what would instantly strike one as improvements in the method are not followed by any better results. Thus, Flatow [3] precipitated the serum, using acetic acid and potassium oxalate, and obtained the whole substance instead of the small amount which will pass through the dialysing shells; he finds that all blood, whether from man or from the pregnant women, will digest placental tissue. Michælis and Lagermarck got similar results, using colloidal iron as a precipitant. On the whole, it seems most likely that the apparently useful results obtained by some observers are due to expectation errors, and that when they have no idea of the nature of the case from which the blood has been taken, their results will cease to be of any value. This is not surprising in view of the very minute indication on which the diagnosis is based, whether the dialyzation method or the polariscope is used, and it does not by any means imply fraud. But the question cannot be regarded as settled, and calls for further investigation.

A paper of the greatest possible importance in this connection has recently been published by Bullock,[4] whose results strike right at the foundation of the Abderhalden theory, on which such a marvellous superstructure has been reared. Bullock's results are of importance, because the experimental method was so carefully devised and so fenced in with controls at every point, that his results may be said to prove themselves. According to Bullock it is impossible to cause the production of a ferment in rabbits which will break down egg-white by the injection of egg-white by any route; this is a simple case, and one in which, if Abderhalden's theory were true, it should be easy to demonstrate such an enzyme. Further, the serum of the pregnant rabbit is unable to break down rabbit placenta, and the serum of the pregnant bitch is unable to break down dog placenta. Blood serum from a

pregnant woman will break down human placenta; but so will that from the healthy male. The blood serum of rats and guinea-pigs breaks down cancer-tissue, but the serum of the guinea-pig was not altered in this respect by a previous injection of cancer-tissue. Similar experiments have been recorded before, but the care with which Bullock's work has been carried out, and the way all obvious fallacies have been avoided, renders his paper tolerably conclusive.

COMPLEMENT DEVIATION IN TUBERCULOSIS.

Two highly important papers dealing with this subject have appeared recently, and it would appear that in careful hands the method has a definite clinical value. Messrs. McIntosh, Fildes, and Radcliffe, after a study of various antigens came to the conclusion—which is what might have been expected on theoretical grounds—that the best results were obtained by the use of a living cultures of tubercle bacilli. A suitable strain has to be procured, and is emulsified in normal saline for use. The actual technique follows fairly closely that of the Wassermann reaction, as performed by Messrs. McIntosh and Fildes [5]; the amount of antigen used is a quarter of the quantity which will give complete absorption of complement in 1½ hours without the addition of serum. Some of their results may be quoted :—

	Positive.	Negative.	Per cent.
Pathologically certain cases of phthisis -	33	10	76·7
„ „ surgical tubercle -	21	5	80·7
„ „ tuberculous glands -	6	10	37·5
Clinically certain cases — phthisis and pleurisy.	10	8	55·5
„ „ „ surgical -	30	12	71·4

Seventy cases, presumably non-tuberculosis, were examined as controls, and all were negative, except two cases of leprosy and one of Addison's disease—which might almost have been put in the tuberculous group. Eighteen syphilitic cases with positive Wassermann reaction were negative, a fact of great importance, for some antigens which have been used act as antigens for the Wassermann reaction as well.

Inman[6] has published a careful study of complement fixation in tubercle by the use of Besredka's antigen, which is prepared by cultivating tubercle bacilli in a fluid medium, containing veal broth and the white and yellow of eggs. The cultures are autoclaved at 115° C., and filtered free from bacilli. The antigen apparently is not easy to prepare. The technique followed on the usual lines, the dose of complement to be used being ascertained by titration with a known normal serum. All the tests were carried out quantitatively, using progressive dilutions of the serum to be tested. Inman obtained very good results in cases of tubercle of the lungs; thus, out of 100 cases, in which bacilli were present in the sputum, no less than 95 per cent. gave a positive reaction in low dilutions, and 40 per cent. in high dilutions; only five were altogether negative. Besredka's antigen does not appear to give such good results in surgical tubercle, and has the disadvantage of acting as a Wassermann-antigen.

Debré and Paraf[7] have attacked the problem in an unusual manner, though one not quite new. Instead of searching for a complement deviating substance in the blood by using known tuberculous material as an antigen, they used a known anti-tuberculosis serum from the horse, and sought for specific antigen in the sputum, urine, and exudates from tuberculous and other cases. They claim the method to be of great value, especially in the diagnosis of tubercle of the kidney in which the urine almost constantly gives positive results. The same is true of tuberculous exudates from the joints, pleura, etc., but the method has not proved of value in the examination of cerebro-spinal fluid or blood. A few experiments carried out in my laboratory by Dr. Ridge, two years ago, using the serum of a patient who had received numerous injections of tuberculin as an amboceptor-serum, seemed to give very encouraging results, and the method warrants further trial.

PROGNOSIS IN PULMONARY TUBERCULOSIS.

Metzger and Watson[2] have studied the urochromogen reaction of Weisz in the urine of phthisical patients, with a view to determining its use in prognosis. They take 1 cc. of urine and 2 cc. of distilled water in each of two test-tubes, and

add three drops of $\frac{1}{1000}$ solution of potassium permanganate to one, which is shaken thoroughly and compared with the control tube. A positive reaction depends on the production of a yellow colour, the solution remaining clear. They hold that it is of distinct value, being of unfavourable prognostic import, and its persistence in spite of proper treatment indicates a hopeless outlook. Its absence is a favourable sign, and so is its disappearance on treatment. It is useless in diagnosis, for it is never given in incipient cases

A NEW METHOD OF PREPARING AGAR CULTURE MEDIUM.

One of the results of the war has been the necessity placed on English scientific workers of replacing many materials, which previously had been imported from enemy countries; in most cases, this has been done without much difficulty. A good example is the case of agar culture medium, the great stand-by of the bacteriologist, which has been made in the past by the use of Witte's peptone almost exclusively, not because it was better for the purpose than any other, but because it was the first to be recommended; the supply of this has now ceased. This apparent inconvenience has been turned to a blessing by the introduction by Captain Douglas[9] of a new medium, which is made entirely (except for the agar) of materials produced at home. It has the advantage of being a much better culture medium for most organisms, and is of especial value when large amounts of bacterial growth have to be produced, as in the preparation of vaccines.

It is prepared as follows. The muscular part of bullocks' hearts is minced, and water added in the proportion of four litres to one heart. The mixture is stirred, made faintly alkaline to litmus, heated to 70°-80° C., cooled to 45° C., and 1 per cent. of trypsin solution added. (Allen and Hanburys' liquor trypsinæ co. is used.) This is allowed to act for two or three hours in an incubator at 37° C. The fluid is next made slightly acid with acetic acid, and brought to the boil; the precipitate is then filtered out through muslin. The filtrate is made alkaline to litmus again, ·5 gram of calcium chloride and 10 grams of salt added (to the four litres), and the mixture autoclaved for an hour at 115° C., the agar being first added.

The prolonged autoclaving brings this thoroughly into solution, and precipitates the phosphates. It is filtered, tubed, and sterilized in the usual way. Agar thus prepared is very clear, and I can quite confirm what Captain Douglas claims for it.

The same author has also described a peptone-free medium for the cultivation of the tubercle bacillus.

RAPID MOUNTING OF FILM-PREPARATIONS.

When large numbers of films have to be examined after a simple process of staining, Willson [10] suggests the use of a solution of gelatin, to which about one-third of its volume of stain is added. The film is spread on a coverglass, dried, fixed, and dropped on to a slide, on which a few drops of this melted gelatin have been placed. The solution stains as it sets, and gives a preparation which lasts a sufficient length of time for ordinary diagnostic work. An oil-immersion lens can be used. When finished with, the slides can be cleaned by simply washing in warm water.

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CANCER OF THE BREAST.

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In the following report on one hundred cases of cancer of the breast, which have come under my care in the last seven years, I have not kept closely to statistical methods, but have endeavoured to emphasize those points which, I believe, are of clinical and practical importance.

On one essential factor, however, extreme care has been taken with the figures, and that is that no tumour, not definitely proved to be carcinoma by microscopical examination by an expert pathologist, has been included in these cases. Every lump from the breast, which I have removed during the seven years I have been collecting these cases, has been carefully examined with the microscope, and in every place where my own figures are given, the accuracy of the pathological description may be accepted.

INCIDENCE.

In 1910, 3,245 female patients were admitted to the London Hospital and amongst these were 107 cases of carcinoma of the breast—that is 3·3 per cent.

Not much reliance can be placed on these figures; for if one surgeon is interested in these cases, an undue proportion is admitted to the hospital. Of more importance is the fact that, in women, the breast is the second most common site of cancer—the uterus standing first.

At the same time, cancer of the breast cannot be considered a common disease. A busy practitioner can easily go for a year or two without seeing a case, and I am assured by a practitioner with a large practice in the East End of London that he has only seen two cases in the last 11 years.

As regards the proportion of cases of cancer to other tumours of the breast, some interesting conclusions can be

drawn from my figures. During the time I was collecting the 100 cases of cancer, I operated upon only 36 cases of other varieties of tumour, including cases of chronic interstitial mastitis. The general statistics of the London Hospital are 107 cases of cancer to 63 cases of all other tumours during the year 1910. Cancer is, therefore, not only the most common of all breast tumours, but is nearly twice as common as all the other varieties of tumour put together.

Age.—My youngest patient was 23, and the oldest 78, the average age being 47. I have had one case—upon whom I did not operate and is therefore not included—of a patient of 91. Eighty-six of the patients were over 35 years of age, and during the period of collection of the patients I only operated upon nine patients with other varieties of tumour, who were over that age. A tumour occurring in the breast of a woman over 35 is, therefore, much more likely to be cancerous than not.

Marriage.—No definite connection between cancer and marriage, pregnancy or suckling could be made out, but the cases with the shortest histories were, on the whole, seen in the unmarried.

Previous Abscesses.—Three cases had had abscesses in the breasts some years before the appearance of the cancer. In two of the cases, the cancers were not in close relationship with the scars, and in the third the abscess was in the opposite breast. I do not think there is any relationship between abscess in the breast and cancer.

Injury.—In none of the hundred cases was there a *definite* history of injury preceding the appearance of the tumour. Some of the patients gave injury as a cause, but on close cross-examination in every case the history was vague. It usually came to the statement that the lump was discovered and the patient must have had a blow, because she could think of nothing else to account for it. In three cases, a definite blow, received a week or two before the patient was seen, was put down by the patient as the cause of the disease, which had obviously been present for months. The blow had led to examination of the breast and discovery of the tumour.

Relationship to Adenoma.—Simple tumours of the breast

are nowadays removed as soon as they are diagnosed, so it is impossible to say whether simple adenomata would in time become carcinomata. In one case, a patient had had an adenoma diagnosed 16 years before I saw her; it had grown very slowly, still retained its innocent characteristics, and microscopical examination showed no traces of carcinomatous change.

Relationship to Chronic Interstitial Mastitis.—I do not think there is or should be any trustworthy *clinical* evidence to support the theory that a patch of chronic interstitial mastitis may become carcinomatous. To get such evidence, a series of cases would have to be watched by skilled clinicians for a number of years, and such a procedure is contrary to all modern teaching. The evidence generally used is "This is a case of chronic interstitial mastitis which I have had under treatment for six months, as the skin is now adherent I believe it to have become carcinomatous and the breast should be removed." Such evidence is useless. The differential diagnosis of *early* carcinoma from a case of chronic interstitial mastitis is in many cases impossible, and the above statement is often a loophole to escape from admitting the error of a wrong diagnosis.

The *pathological* evidence is, however, I think, conclusive. Microscopical examination of a breast, the site of a carcinoma, frequently shows that chronic interstitial mastitis is present in an advanced degree, and, on the other hand, examination of cases of mastitis show marked proliferation of the cells of the acini which in some cases have penetrated the basement membrane so that a carcinoma is already present. These cases are frequently typical clinical specimens of chronic mastitis. It may be accepted, therefore, that carcinoma not infrequently arises in a patch of chronic interstitial mastitis.

HISTORY.

In 67 of the 100 cases, the lump in the breast was discovered by accident, the most common statement being: "I noticed a lump in the breast whilst washing." In 10 cases, pain of a slight nature caused an examination of the breast. In three, there was a blow which led to discovery, and in three others, the patient noticed nothing until the skin over

the tumour became discoloured. The absence of pain is a marked feature in the history of cases of cancer of the breast and the chief cause of late diagnosis. A patient will frequently give a history of a lump being in the breast for a year or 18 months, and when asked why she has not sought advice before says: "Oh! It caused me no pain, so I thought it did not matter." In cases of chronic interstitial mastitis, on the other hand, pain is often a marked feature. It is frequently the pain alone that causes the patient to seek advice, and the pain becomes aggravated at each menstrual period. It may be stated as a general rule that the more the patient complains of pain in connection with a lump in the breast the less dangerous is the condition.

In four cases, the patient came for advice for a discharge from the nipple, but three of these patients had been aware of the lump in the breast for some months; in the fourth case, the discharge, which was blood-stained, was the only physical sign, and it was only on operation that a small duct carcinoma was discovered.

I have had under my care three patients suffering from spontaneous fracture, due to secondary cancer in the bones; but all three had been aware of a lump in the breast for some months, and had not sought advice because it was painless. Another curious case was a woman who sought advice for erysipelas of the arm. She had a large ulcer the size of a cheese plate covering the left side of the chest and exposing three ribs. She stated that five years previously she had had a lump in the breast and that she had painted the chest with iodine every day until the whole of the breast had sloughed off, and that she had removed "kernels" from the axilla. On post-mortem examination, carcinoma was found in the mediastinal glands and lungs.

CLINICAL FEATURES.

A cancer of the breast with the text-book clinical features, viz., a hard solitary tumour in the breast, adherent to the skin, fixed somewhat to the pectoral muscle, causing retraction of the nipple, and associated with a hard enlarged mass of glands in the axilla, can hardly fail to be diagnosed accurately. Unfortunately, many of our patients do not come

to see us until this stage is reached. It must, however, be understood that all these signs are late, and mean that the disease is advanced; but the diagnosis of cancer *must* be made before any of them are present, if the patient is to have the best chance of freedom of recurrence after operation. Not only are these signs late, but the disease may be advanced without any of them being present. In one of my cases—a woman of 34—there was a lump in the breast, partly cystic and partly solid, which was freely movable, not adherent to the skin or pectoral fascia, and the nipple was not retracted. It was a cancer, the centre of which had already broken down, and, in spite of free removal, an extensive recurrence occurred in 18 months.

The early diagnosis of cancer of the breast must therefore be made by other means than the usual text-book physical signs, and it is of the utmost importance that a patient with a tumour of the breast should not be watched until one or more of them appear.

It may be stated at once that, if a woman over 30 has a solitary solid lump in the breast, cancer is by far the most likely diagnosis, and that that diagnosis is made almost certain if the lump alters the contour of the breast. A cancer, by the contraction of the fibrous tissue in it, draws the breast tissue together making it slightly more prominent, and tends to elevate the nipple. If these signs are present, the diagnosis of carcinoma may be made without hesitation, no matter how freely movable the lump may appear to be.

The greatest difficulty will arise in distinguishing a cancer from a patch of chronic interstitial mastitis. In typical cases, the difficulty is not great. In cancer, there is a hard solitary lump, whilst with mastitis there are two or more lumps in the breast and often involvement of both breasts, the lumps are ill-defined, often confined to one lobule of the breast and frequently cysts are detected in them.

In other cases, however, when there is only one lump in the breast, the differential diagnosis by clinical means is impossible. One of my patients, a woman of 25, presented herself for examination with a lump in the axillary lobe of left breast. It felt knotty, and was believed to contain small cysts. It was not adherent to the skin or pectoral fascia, the

nipple was not retracted, and the remainder of the breast and the right breast felt granular. The condition was diagnosed as mastitis, but microscopical examination after removal proved it to be cancer.

Bilateral cases of cancer are not very uncommon. In two of my 100 cases the patients had carcinoma in each breast when first seen, but the physical signs of the tumours left no doubt as to their nature. In five cases, recurrences occurred in the other breast after removal of one for cancer.

DIAGNOSIS.

The diagnosis of a cancer of the breast, when the usual text-book signs are present, is one of the easiest of surgical diagnoses, and can often be made at a glance; but in early cases, a certain diagnosis from other tumours of the breast, especially from chronic interstitial mastitis, by clinical signs alone is not possible. It is therefore necessary to formulate rules for the treatment of tumours of the breast so that, on the one hand, unnecessary operations are avoided, and on the other, only a minimum of time is lost, if the case proves to be one of cancer.

When a patient comes for advice for a lump in the breast, a careful examination should be made, and if the diagnosis is doubtful (and these are the cases under consideration), the case may be treated as one of chronic inflammation for not longer than three weeks. If the lump has not disappeared or become considerably smaller in this time, operation should be advised and consent to remove the whole breast, if necessary, should be obtained.

At the operation, a wedged-shaped piece of the breast containing the lump should be removed, and this is at once examined macroscopically. In the majority of cases, the diagnosis is at once established, but if doubt still remains, the wound is sutured, and a microscopical examination carried out. Should the case be one of cancer, the whole breast is removed at an early date.

American surgeons and pathologists have strongly objected to this method of dealing with those tumours that cannot be diagnosed by macroscopical examination. They insist that an immediate microscopic examination of a frozen section should

be carried out, so that, if necessary, the complete operation can be performed at once. They state that delay of a few days makes the prognosis of radical cure practically hopeless. If this microscopical examination cannot be carried out, they advise the complete operation in doubtful cases, for the case is more likely to be cancer than not. I have carried out immediate microscopical examination of breast tumours, but this is, for obvious reasons, not always possible, and the pathologists I have chiefly worked with do not like to give a definite opinion in a doubtful case on a frozen section. It is often necessary, in making a differential diagnosis, to cut sections of various parts of the tumour, and obliquely cut sections of chronic degeneration closely resemble cancer.

The cases in which macroscopical examination fails to diagnose the tumour are very few, and for the present I use the following rule. If, in my opinion, the case is probably cancer, I perform the complete operation, but if it is probably mastitis, I wait for a microscopical report. In only four of my 100 cases have I had to perform a second operation, and two of these were operated upon early in the series; under the above rule, the complete operation would have been done on the macroscopical appearance.

THE OPERATION.

My routine operation for cancer of the breast is :—removal of an area of skin the centre of which is the tumour, and which always includes the nipple; the subcutaneous tissue from the middle of the sternum to the latissimus dorsi and from the clavicle to well on to the abdomen; the breast; the pectoralis major and minor and their fasciæ (the clavicular head of pectoralis major is frequently saved, pectoralis minor is always removed); the whole of the fat and fascia in the axilla; the fascia over the serratus magnus and the subscapularis. The operation is commenced in the axilla, the insertion of the pectorals being divided, and the axillary vein and artery being carefully cleaned and all their branches tied except the circumflex vessels.

All the fat and fascia with the glands in the axilla are removed in one piece, and it is not until this is done that the breast is touched. The actual removal of the breast and

pectorals is now a matter of a few minutes, the only bleeding of any importance coming from the perforating branches of the internal mammary artery, which come through close to the sternum. All hæmorrhage is then stopped, and the wound closed; if the incisions have been carefully planned, there is never any difficulty in bringing the edges of the skin together. A small drainage tube is placed in the axilla for 48 hours. The entire operation takes from ¾ hour to 1¼ hours, the time depending on the fatness of the patient.

The arm is bandaged at right angles to the side, and supported on a pillow until the drainage tube is removed, after this the patient is encouraged to move the arm. The stitches are removed on the eighth day, and the patient usually leaves the hospital under a fortnight.

In five cases, I have removed the supra-clavicular glands at the same operation, but I do not think this should be done as a routine. I have removed them in cases in which I have found numerous slightly enlarged glands in the axilla at the time of operation.

MORTALITY.

My mortality for the 100 cases is 3. One patient had a goitre, and did not recover consciousness. The second, an elderly lady, died quite suddenly after the stitches were removed, and was found on post-mortem examination to have extreme fatty degeneration of the heart. The third was a woman of 42, who died suddenly of pulmonary embolism, whilst having tea with her friends on the seventh day after the operation.

RESULTS.

The majority of my cases have been the wives of working men, and in no case has the loss of the pectorals been more than a trifling inconvenience. All say they can do their house work as well as before the operation. There is slight limitation of movement of the arm upward due to contraction of the scar. Some patients complain of slight pain on the inner side of the upper arm, due, I believe, to involvement of the internal cutaneous nerve in scar tissue, but the pain is never serious. A few cases have slight œdema chiefly of the back of the hand, and at the back of the elbow. It may be

stated generally that the inconveniences resulting from the operation are trifling.

PROGNOSIS.

A statistical review of my 100 cases would be of little value. Some are of quite recent date, others were so advanced when first seen that palliative operations only were undertaken, and other patients have been lost in the usual way the hospital patient disappears.

I have chiefly been struck with the great difficulty in giving a prognosis in any particular case. Generally speaking, the earlier the case is seen the better the prognosis, but great caution should be shown in forecasting the result of any particular case.

One of my patients was a woman of 28, who was pregnant, and who had a huge cancer growing rapidly. I expressed the opinion that operation was undesirable, but consented to do it at the urgent request of the patient and her friends. Five years later she was playing the piano at a concert. Another case was a woman of 50 with a small scirrhus growth recently noticed, not attached to the skin or fascia, and no glands were felt in the axilla. Complete excision was carried out, and favourable opinion expressed about recurrence. A year later she had extensive recurrence all over the skin of the chest.

Another curious feature of recurrence is the frequent rapidity of growth after a period of freedom. As far as possible, I see my cases every month in the first year after operation, and every third month afterwards. It is by no means uncommon to examine a patient and find no trace of recurrence anywhere, and for her to come up in a month or three months with a quite inoperable recurrence.

Out of my 100 cases I have so far performed 11 operations for recurrence, 5 locally in the skin, 4 in the supra-clavicular glands, and 2 in the opposite breast. Recurrence in the lungs has been seen five times, the patient first complaining of a dry cough, and then developing signs of solidification of the lungs or fluid in the pleura. In one case, there was recurrence in the dorsal spine, but I have not seen any other case of recurrence in the bones.

In two cases, recurrence in the skin occurred five years after

the original operation, but in one of these the secondary growth was removed, and at the time of writing there is no further recurrence.

CONCLUSIONS.

On thinking over these 100 cases, the chief impressions left are :—

(*a*) The late stage at which these cases are usually seen, chiefly due to the patient taking no notice of the lump because of the absence of pain. A patient not infrequently has noticed a lump for one or two years before seeking advice.

(*b*) The great difficulty or impossibility of diagnosing clinically between early carcinoma and a patch of chronic interstitial mastitis.

(*c*) The rapidity of the convalescence after the operation.

(*d*) The slight amount of inconvenience and disability following the operation.

(*e*) The difficulty in giving a prognosis in any particular case.

RADIUM.

My experience of radium is limited to two cases, both of which were inoperable. Neither received the slightest benefit from the treatment. In one case, the application was given at the Radium Institute, so it may be assumed that the treatment was very thorough.

X-RAYS.

I have had eight cases of recurrence treated by X-rays, and have seen temporary improvement in several of them. In one case, a large mass appeared in the opposite breast after removal of one for cancer. This mass had all the clinical characters of a cancer, and I had no doubt of the diagnosis. It completely disappeared under X-ray treatment, and later the patient died with recurrence in the thorax. Some of my cases have had a six weeks' course of X-ray treatment after the breast has been removed, but I have no figures yet showing the advantages or disadvantages of the procedure. In two cases of recurrence in young subjects, I removed the ovaries, but neither case derived any benefit.

RECENT WORK IN URINARY SURGERY.

By J. W. THOMSON-WALKER, M.B., F.R.C.S.

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BLADDER.

THE treatment of papilloma of the urinary bladder with the high-frequency current, introduced by Beer, of New York, in 1910, has been the subject of a few articles.

Ashcroft[1] holds that the bipolar or d'Arsonval current is superior to the unipolar or Oudin current. This observer experimented with raw beef and liver, and found that to produce the same amount of destruction in each of these, a current of greater strength was required under water than in air. He considers that the unipolar current, when applied through a cystoscope, has but a limited field of usefulness, which is confined to small papillary tumours. When dealing with larger growths, or those suspected of malignancy, the bipolar current is indicated. He has seen growths proliferate rapidly under the unipolar current.

In using the bipolar current the first application should last 15 seconds (250 ma), then a rest of 15 seconds. The currrent is again turned on for 15 seconds (300 to 350 ma). As the patient grows accustomed to this treatment, the strength can be increased. Some patients complain of pain with a moderate current, while others bear a strong current without discomfort.

Each *séance* should consist of at least six applications of 15 seconds each, with a rest of 15 seconds between, and at least two areas should be treated. The fluid in the bladder may become uncomfortably warm; its temperature has been found to vary from 105° to 115° F.

Except in the case of a carcinoma, there is little if any reaction. There may be a little pain, which is readily controlled; there may be a slight rise of temperature as well. Sometimes in carcinoma, there is a severe reaction such as a rapid rise of temperature and pulse, and the appearance

of constitutional symptoms, but these usually disappear quickly. The amount of reaction will act as a guide for the interval between the treatments. Usually the treatment is repeated once a week, but in some cases a 10 days' interval is necessary.

H. Gehrels[2] strongly advocates the use of this method in papillomata of clinically benign appearances, if they do not exceed the size of a walnut, even if they are multiple; in all recurrences of papillomata, either after endovesical treatment or after cystoscopy; and in cases of hæmorrhage from malignant growths that cannot be arrested by the usual means. The choice of the right cases is the most difficult point in the whole question of the endovesical treatment by high frequency. There are difficult cases of malignant growth resembling simple papilloma. In making the diagnosis, the author depends upon the age, youth being in favour of benign growth. Long intervals between the hæmorrhages being also a sign of simple papilloma. Pain is rare in benign cases, the outflow of urine is not disturbed, and the general health is not affected. Cystitis is easily cured in simple papilloma, but is persistent in malignant growth. Cystoscopically, the malignant growth is likely to be smooth, with a broad pedicle, and there may be signs of infiltration of the mucous membrane.

Bladder Tuberculosis.—Edward Keyes, junr.,[3] holds that there are cases secondary to inoperable prostatic or bilateral renal lesions, and other cases persisting after nephrectomy, in which neither general treatment nor time gives relief. Tuberculin seems to alleviate the bladder symptoms in certain cases, but it is slow, and has been uncertain in this author's experience. Local treatment is occasionally effective in relieving the painful symptoms. He adheres to the following principles in the treatment of such cases:—

1. The instrument must not enter the bladder. A Guyon spring is used, and is introduced into the prostatic urethra. The solution is injected, and flows into the prostatic urethra and the base of the bladder.
2. The injection must give relief in proportion to the pain which it inflicts. The author uses the following solutions:—Thallin sulphate, gomenol,

bichloride of mercury, and carbolic acid.

Thallin sulphate is used in a saturated solution in water (20 per cent.), and is much less irritating than a solution of 1 in 1,000 of nitrate of silver. It usually gives no relief whatever, but occasionally it is efficacious. Gomenol, though greatly praised by some, has not proved successful in the author's hands. Bichloride of mercury has been of great service. It is used as an instillation, the initial dose not exceeding 1 in 20,000. This is repeated daily, and the strength increased rapidly up to 1 in 10,000 or 1 in 5,000, when irritation is usually experienced. The intervals are then increased to two or three days, and the amount of water diminished, so that one, two, or three drops are injected.

Carbolic acid was recommended by Rovsing, who employs an irrigation of 5 per cent. solution, the bladder being repeatedly injected and emptied. The pain caused by this treatment is considerable. Keyes uses carbolic acid as an instillation, instead of an injection, in solutions varying from 0·5 to 1 per cent. He finds no great benefit, until the strength reaches 2 to 5 per cent.

URINARY ANTISEPTICS.

The antiseptic action of hexamethylene-tetramine (hexamine, urotropin), in the urine, the method by which it is produced, and the causes of variation in the action, are of extreme interest in urinary surgery.

Hexamine is a condensation product of ammonia and formaldehyde, and in solution has no antiseptic action. There is no longer any doubt that its antiseptic power in the urine is entirely due to the splitting off of formaldehyde in that acid medium. The difficulties that hampered the earlier investigators in this line, were due to the fact that the tests at their disposal did not discriminate between hexamine and free formaldehyde. This difficulty no longer exists, for the recently introduced Rimini-Burnam tests demonstrates the presence of free formaldehyde, and distinguishes between this and formaldehyde in combination as hexamine.

The following is Burnam's modification of Rimini's test:— Three solutions are used:—

(1) Phenylhydrazine hydrochloride, 0·5 per cent. (2) So-

dium nitroprusside, 5 per cent. (3) Sodium hydrate, saturated solution. Three drops of each of the first two solutions are added to the urine, and a few drops of the sodium hydrate solution poured along the side of the test tube.

If formaldehyde is present, a greenish black colour passes down through the urine, and clouds the fluid. This rapidly changes to green, and fades through light green to orange and pale yellow. The urine and the sodium hydrate should be warmed to slightly above body temperature. This test will detect formaldehyde in urine, in a dilution of 1 in 150,000, but does not show the reaction with hexamine.

According to Burnam, there is an intense dark blue colour, changing to green, in solution of 1 in 20,000 or stronger, and in solution of less strength the first colour is an intense green.

If the test is negative, a fresh sample should be boiled after the addition of a few drops of sulphuric acid. The test is then applied, and if the formaldehyde reaction is present, the urine has contained hexamine. By the use of this test, important observations have been made on the conditions under which hexamine liberates formaldehyde, and therefore acts as an antiseptic agent in the urine.

The following points are from an article[4] by the present writer :—After a dose of 10 or 15 grains of hexamine, the drug or formaldehyde can be detected in the urine in about an hour, but it is frequently delayed longer than this, two, or even three hours being not unusual. The excretion is at its maximum during a period of from four to eight hours after admininistration, and after 12 hours, excretion is still going on in small quantities. It would be possible, by taking two doses of 15 grains in 24 hours, to keep the urine in the bladder continuously mixed with a strong solution of formaldehyde. In diseases of the bladder, in which frequent inclination is a symptom, the period during which the bladder is under the influence of formaldehyde is reduced to about six or eight hours, during which time the drug is being excreted by the kidney. In such cases small doses, frequently repeated, will be more effective in giving a continuous antiseptic action.

A dose of five grains three times daily is usually too small to produce formaldehyde in the urine, and doses of 10 or 15 grains are preferable. Formaldehyde is not split off from

hexamine in an alkaline urine, and the latter should not, therefore, be prescribed with an alkali. The beneficial effect of alkalis on the symptoms in bacillus coli infection of the urinary tract is due to a neutralization of an acid toxæmia, produced by the bacteria; they have no influence on the bacteria.

In all acute colon bacillus infections, it is advised that alkalis should be administered until the symptoms subside, and then hexamine should be given in increasing doses, until the formaldehyde reaction in the urine is fully developed.

Diluents such as Contrexéville, Vittel, and other waters, reduce or completely destroy the effect of hexamine in the urine, and the same effect is brought about in cases in which polyuria from disease is present. It is advised that hexamine should be given, and formaldehyde detected in the urine, before all operations on the urinary tract, as well as those involving the bowel and the pelvic organs, as a prophylactic measure against infection.

When some pathological condition, such as stone, enlarged prostate, etc., is present, in addition to the urinary infection, the urinary antiseptic will not take effect until the stone or other lesion is removed.

It is recommended that the reaction of the urine should be tested before administering hexamine, and that it should, if necessary, be rendered strongly acid by the administration of sodium acid-phosphate or ammonium benzoate.

The Rimini-Burnam test should be used in every case, to ascertain if formaldehyde is being produced in the urine.

George C. Smith,[5] after an investigation of the excretion of formalin in the urine by the use of this test, comes to the following conclusion. Burnam's test for formaldehyde in urine is definitely positive, when this substance is present in the strength of one part in 40,000 or more.

The urine should be examined as soon as possible after it has been voided. A negative test, at any time, does not prove that formaldehyde is never liberated. Formaldehyde is liberated from hexamine by the acids of the urine. The process may take place in the kidney, but is continued in the bladder. Litmus paper was unreliable as a true indicator of the acidity of the urine in about 25 per cent. of cases. The degree of acidity, as measured in terms of its hydrogen in

concentration, showed a constant relation to its power to set free formaldehyde.

KIDNEY.

Movable Kidney. — Billington[6] defines a pathologically movable kidney as "one the position of which is affected by influences other than respiration, and in particular by gravity." Two tests are applied to ascertain if pathological mobility is present: (1) Is the level of the kidney influenced by gravity? (2) Can the kidney be pushed to a higher level, and can it be prevented from ascending during expiration, by grasping its lower pole? Heredity, he regarded as an important factor in ætiology, and muscular overstrain as the most important direct cause.

In order to obtain full information, the patient must be examined both standing up and lying down. The author favours the method of grasping the loin with one hand, while the other hand is free to palpate the abdomen. When the kidney is movable, the loin is softer and feels empty, and percussion over the renal area posteriorly gives a resonant note. When rotation of the kidney, without downward displacement, is suspected, it may be impossible to palpate the kidney. A diagnosis must be made on symptoms, the signs enumerated, and evidence in the urine of interference with the renal function.

The author distinguishes five groups according to the symptomatology.

(1) The symptoms are local and definitely related to the kidney.
(2) The symptoms are due to functional disturbance of the sexual organs.
(3) Chronic functional disturbances of digestion.
(4) Spinal and cerebral neurasthenia.
(5) Mental derangement.

K. M. Pardhy[7] explains the occurrence of mental disorders in cases of movable kidney, as resulting from a toxæmia produced by—

(*a*) Deficient excretion of waste products.
(*b*) Interference with formation of an internal secre-

tion.

(*c*) Possible formation of a perverted internal secretion.

(*d*) Kinking of the ureter, and stasis of decomposing urine.

This author claims cures in 80 per cent. of cases of mental disorder with nephroptosis, by means of nephropexy. The time taken for complete cure varies from a few months to a year or more, and during this time treatment is carried out on the lines usual in mental cases. The psychic symptoms are worse immediately after the operation, and sometimes for a few weeks afterwards.

A much more moderate estimate of the effect of nephropexy in this class of cases is given by Billington. "I wish to emphasize the fact that nephropexy does not cure the patient, except when performed for purely local symptoms; it only makes it possible for recovery to take place."

Fowler[8] holds that the lower calyces are imperfectly drained, even in the normal position of the kidney. In movable kidney, he performs an operation by which the kidney is rotated upon its antero-posterior axis, so that the upper pole is drawn downward, and the lower pole drawn outward and upward, so that the lower calyx is on a level with, or beyond the upper calyx. When in the upright position, the urine would have a downward gravity flow from the lower, as well as from the upper pole. To support the organ in this position, Fowler uses two strips of fascia lata, one half inch wide and 11 inches long, from the outer aspect of the thigh. Bridges of renal capsule are raised at each pole, and the strips woven through, and the ends brought out through the muscles of the back, and the kidney fixed in a nearly transverse position.

In a discussion on nephropexy and its results, at the Royal Society of Medicine,[9] G. Percival Mills gave the following results in a series of cases operated on in the General Hospital, Birmingham. (See table on page 759.)

The author stated that the advantage of operations (*b*) and (*c*) was obvious from these figures; for, though (*d*) showed fewest relapses, it usually resulted in a low fixation, associated with a bad functional result. The great majority of relapses

occurred during the first two years.

—	Fixed high.	Fixed low.	Relapsed.
(*a*) All cases	53 per cent.	23 per cent.	23 per cent.
(*b*) Fixed to rib and capsular suspension suture.	73 „	0 „	26 „
(*c*) Suspension suture only	62 „	12 „	25 „
(*d*) Sutured to muscles of loin	12 „	75 „	12 „

The functional results, tabulated from statements by patients, were as follows :—Gross results, 57 cases, 33 per cent. cured; cases with lumbar pain only, 34 cases, 50 per cent. cured; neurosis, 21 cases, 9 per cent. cured; cases of uncomplicated lumbar pain relieved by horizontal rest, 20 cases, 75 per cent. cured; cases of uncomplicated lumbar pain unrelieved by horizontal rest, 10 cases, none cured.

The following were his conclusions :—

(1) The general results of nephropexy were bad.

(2) The operation was frequently performed to relieve symptoms that were not due to movable kidney, and these symptoms persisted after a mechanically successful operation.

(3) The symptoms due to a movable kidney were chronic lumbar renal pain, relieved only by horizontal rest. These symptoms, if present alone were nearly always cured by nephropexy.

(4) When lumbar pain was associated with neurotic symptoms, nephropexy rarely gave relief.

(5) Nephropexy failed to cure cases of dyspepsia, supposed to be due to obstruction of the duodenum by a right movable kidney.

(6) The following were the indications for nephropexy :—

(*a*) Intermittent hydronephrosis.
(*b*) Pain of character described.
(*c*) A few cases of Glénard's disease.

Thomson-Walker said the results of operation depended very closely upon the proper selection of cases. Cases were divided into (1) those with symptoms directly connected with

the kidney, such as renal pain, hæmaturia, casts, albumen ; (2) Those in which there were symptoms not directly connected with the kidney, viz.: (*a*) Gastro-intestinal symptoms, and (*b*) Nervous symptoms. In class (1) the results of operation, if it was mechanically successful, were uniformly good. In class (2) with gastro-intestinal symptoms, there were frequently extensive adhesions around the cæcum and colon. The cases in this class that were likely to do well after nephropexy, were those that were benefited by rest in bed, and made worse by exercise. The results in cases of neurasthenia were very unsatisfactory. The majority of operations performed for movable kidney did not completely fix the kidney, and if movement were permitted there was no method of controlling it, or preventing movement taking place in some unexpected direction. He fixed the decapsulated posterior surface of the kidney on the carefully denuded muscles of the posterior abdominal wall. The anterior surface was not stripped, as it would then adhere to the bowel. The evidence produced to show that a low fixation was the cause of failure, was of the most flimsy character. So long as there was no dragging on the vascular pedicle, and no twisting or other obstruction of the ureter, and the kidney lay internal to the outer border of the quadratus lumborum, there was no reason to believe that a low position would cause symptoms.

Gardiner presented the statistics of cases operated upon at Guy's Hospital for four years (1909-12). There were 26 operations; 21 patients were relieved; five were not completely relieved. Blakeway gave the results obtained at St. Bartholomew's Hospital during the same period. There were 62 cases, 59 female and three male. There were two bilateral operations. There was one fatal case (chronic interstitial pneumonia); and 26 were not traced. The results were satisfactory in 22, unsatisfactory in 12, and successful in one side in one. Of 14 cases examined, six were satisfactory as regards symptoms, but in two of these the kidney was still mobile; eight were unsatisfactory. Johnson read statistics from St. Thomas's and St. George's Hospitals, for the same period. At St. Thomas's Hospital 53 had been operated upon; 32 of these had replied to inquiries as follows:—Good, 16; fair, 4; poor, 2; temporary relief, 1; failure, 9. At St.

George's Hospital 24 patients had been operated on, but only eight were traced. Of these three were worse, one was unchanged, and three slightly improved, and only one was completely recovered. The kidney had remained absolutely fixed in only one case.

Luzoir [10] records 35 cases of movable kidney operated on by Albarran's method of utilizing flaps of capsule, modified by Marion, so that the lower part of the capsule is not detached from the kidney, and forms a sort of hammock which supports the organ, and the kidney is fixed higher up. The upper flaps of capsule are fixed above the eleventh rib. Luzoir obtained information with regard to Marion's end results in 28 patients. One case was a failure due to mistaken diagnosis, and was excluded. The other 27 patients had pain in the kidney region. Of these 15 were relieved of pain, 12 were improved, but continued to suffer abnormal pain, the cause of which was found in the genital system in one, in the appendix in two, in the gall bladder in one, in the stomach (ulcer) in one; four patients had enteritis, and three had movable left kidneys. Sixteen of the patients had nervous troubles, which disappeared completely in three, were very much improved in four, improved in six, and there was no improvement in three cases. Nineteen patients had digestive disturbances, which in six cases disappeared entirely, one case was very much improved after a later appendicectomy, nine cases showed slight improvement, and in three there was no improvement.

PROSTATE.

Legueu and Morel [11] studied the blood in 85 patients suffering from various diseases of the prostate, and found that the leucocyte count varied with the nature of the disease. An increase in the eosinophile count was specially noted in 90 per cent. of cases of adenoma. Apart from the effect of any parasitic toxæmia, or medicine, the increased leucocyte count was present in 5 per cent. of cases of adenoma of the prostate, which were not infected, and did not suffer from hæmaturia. It was apparently due to the adenoma, for it disappeared after operation, and further histological examination of the adenoma showed an abnormal proportion of eosinophiles in the peri-urethral zone. Although the eosinophilia in prostatic cases, is

not a specific reaction, it has a real diagnostic value. It may settle the question of diagnosis between a neoplasm and an adenoma, and reveal, in cases of prostatic symptoms without enlargement of the prostate, the presence of minute adenomata.

Marion[12] recorded six cases of suprapubic prostatectomy for chronic prostatitis in patients treated for a long time without success by other methods. In these cases the prostatic urethra was not removed, but an incision was made radiating from the urethra obliquely backwards and outwards over each lobe. The finger was introduced into each of these incisions, and the prostate lobes dissected and removed. This, he claims, is easily accomplished. In one case, complete retention of several months' duration was cured. In three cases there was cessation of pain and discharge, and neurasthenic symptoms. In two cases the results were incomplete, discharge stopped, but pain and neurasthenic symptoms persisted. The effects on the genital function was, that erection and sensation were normal, but in two patients there was no ejaculation; the other patients were uncertain as to this point. This is a serious result, and the operation should only be performed when all other methods have failed, and the patients should be warned of the result, beforehand.

Gayet[13] has studied Ambard's urea co-efficient, in a series of 54 prostatic cases, and arrives at the following conclusions:—The co-efficient, by itself, does not pretend to furnish a reliable picture of the anatomical changes in the kidney; it only shows the physiological state of a single function, the elimination of urea. Retention, especially when complete, is an important factor in azotæmia, and the highest urea content in the blood serum, is found in these cases. The removal of the obstacle by a permanent catheter, or cystoscopy, brings about a rapid decrease of the uræmia. The prognosis is only grave if it persists after retention has been relieved.

The urea co-efficient makes it possible to follow very closely the improvement brought about by the relief of the retention, and to choose the best time for radical operation. The method does not always agree with the results of determining the urea of the blood alone. According to this

authority, it is surer and more reliable than the methods by elimination of colouring matter. If it is supplemented by a study of the other renal function, elimination of water, chlorides, etc., and by a study of the patients' other organs, it aids in giving the precise indication for operation.

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FATAL GASTRO-INTESTINAL HÆMORRHAGE IN THE NEW-BORN.

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I THINK all will agree that a disease, which exacts a mortality of from 50 to 80 per cent., deserves the closest study and attention. It is true that the ailment with which this paper deals is not a very common one, but nevertheless it adds appreciably to our already overhigh infant mortality; moreover, so little appears to be known of the pathology of the disease, that it is not a matter for much surprise if our treatment of it, when the occasion arises, has, up to the present, been of little avail. It must be understood that I am not dealing with mere melæna neonatorum, with hæmorrhage of syphilitic origin, with that directly due to injury, nor with cases in which blood has been taken into the mouth. The lesion is what I prefer to look upon as a definite clinical entity, a disease so far of unknown origin, the principal symptom of which is severe gastro-intestinal hæmorrhage, which, in the large majority of cases, proves rapidly fatal.

Before giving the details of my own case, I will briefly sketch a picture of a typical case, and refer to what students of the disease have already recorded in the literature, regarding its possible causation.

Although cases have been recorded in which the birth of the child affected was fraught with much difficulty, and difficult labour has even been suggested as a possible cause of the hæmorrhage, due presumably to trauma of body or brain; yet, in a number of instances, the birth was easy, and the child apparently perfectly normal, in which state it has remained for, perhaps, 24 hours. Then a little vomiting of brownish material, or of blood in small bright clots, occurs, and at the same time the stools become blacker than meconium usually is, and sometimes a little red blood is visible in them. Rapidly and progressively, both stools and vomit contain more and more blood, until both almost entirely consist of it in a more or less

altered condition.

The infant shows all the signs and symptoms of loss of blood. The most prominent of these are: progressive weakness; the lusty cry changing to a whine or feeble moan; the skin becoming dry and dull yellow, although not actually jaundiced; the respirations shallow; the pulse weak, and the extremities cold. Death usually occurs in about five days with a convulsion. The disease appears to be more common in boys, in the proportion of about 2 to 1, and this fact has been quoted in support of the theory that the disease is allied to, if not actually a phase of, hæmophilia. Careful examination of the blood and organs in fatal cases, and the after-history of non-fatal cases, have shown, however, that such is not the case. One case had a circumcision done a little later without ill effect. In others, there has been no after undue tendency to bleed, or no inclination to spontaneous hæmorrhages such as nose-bleeding, etc. Again, we should expect umbilical hæmorrhage if the child were a hæmophiliac, but this has rarely, if ever, been recorded.

The malady is not likely to be mistaken for Winkel's hæmoglobinuria, a disease most probably of infective origin, in which cyanosis, jaundice, and somnolence are well marked. In common with all ailments, a microbe has been "discovered," and credited with being the causative agent. Ten years ago, Gärtner described a melæna bacillus, which he found in two of his cases, but up to the present day his finding remains unconfirmed.

Ulceration of the stomach and duodenum has been looked upon as a cause, as well as marked congestion of the mucous membrane of these organs without actual lesion.

In one case at the autopsy, a small ulcer was found, which had opened into an artery at the cardiac end of the greater curvature of the stomach. In another case, an ulcer was found which had opened into a duodenal artery.

Landau advanced his ingenious theory as to the cause of these ulcers, stating that an embolus became detached from the umbilical vein or ductus arteriosus, and being swept into a branch of the gastric or duodenal arteries, occlusion occurs, followed by necrosis and ulceration, with further tissue necrosis and involvement of blood-vessels with hæmorrhage. This is not a very probable explanation, for the disease does not

appear to be merely local, because, in the last case I referred to, infarcts were found in the lungs and other organs. Capillary defects have been suggested as a cause, but they have never been demonstrated. Syphilis has not been found associated with the disease.

As I have previously stated, the disease under consideration is a definite condition whose cause is unknown. The name melæna neonatorum should be discontinued, as it merely indicates a condition which might as readily, or more so, be due to blood coming from badly cracked nipples in the mother, or from other situations. The black motions are due to the hæmoglobin of the blood being changed into hæmatin, which, in contact with the H_2S of the bowel, becomes a black sulphide of iron. Tarry stools, therefore, only indicate that blood has lain for some time in the intestine. If doubt exists about black motions being due to blood, microscopic examination will reveal some blood-corpuscles if present.

Needless to say, in a disease characterized by so obscure a pathology, the treatment resolves itself of necessity into a symptomatic one. One must endeavour to check the bleeding, whatever its source, and to treat the symptoms due to loss of blood. The latter is the more easily disposed of, because it is called for so frequently in many other types of case, and at all ages. I would lay particular stress, in this connection, upon the necessity of maintaining the body-heat of the infant, and upon saline infusions. For the checking of the hæmorrhage, many measures have been tried, most of them with a doubtful degree of success. Prominent amongst them are styptics, by the mouth and by the rectum, and preparations designed to increase leucocytosis and the coagulability of the blood. The principal ones are:—

Liq. ferri perchlor., in doses of 2 to 3 mins. diluted, every two hours.

Adrenalin, 1–1000 solution, 1–2 mins. in water every hour for three doses, then every 2–3 hours.

Or 3–5 mins. in 2 drachms saline solution *per rectum*.

Ergot has been used too.

The doubtful possibility, that any of these preparations will reach the bleeding point or area with any degree of certainty, makes their employment of little value in an urgent case. Better, perhaps, is the use of gelatin by mouth, and

some good results have been reported from drachm doses, given hourly, of a 2 to 5 per cent. solution, or by 1–2 oz. of the solution by rectum.

A good formula for its administration is as follows :—

Gelatin alb.	-	-	-	gr. xxx.
Sodii Chloridi	-	-	-	gr. ii.
Aq. destil.	-	-	-	ʒiii solve.

Calcium chloride has been given in doses of 2 grs. in water, every two hours, and nucleic acid, thymus gland extract, yeast, etc., have been suggested as producing a marked leucocytosis by reason of the nuclein contained therein.

Again, gelatin has been recommended for subcutaneous injection, and if made absolutely sterile in order to avoid risk of tetanus, and used with the utmost antiseptic precautions, it seems to be the best suggested treatment. From two to six drachms of a 10 per cent. solution are injected two or three times daily, the needle puncture being immediately sealed with care.

The drawback to oral medication is the vomiting, which is usually troublesome. It is desirable even to avoid milk as nourishment, at any rate *cows'* milk fresh or preserved; rather is it preferable to keep up nutrition by means of whey and albumen water, administered almost cold in small amounts at frequent intervals.

In my case, I would not permit suckling, lest the exercise entailed should distress the weakly infant or raise its blood-pressure, and thereby increase the bleeding.

CASE.

In briefly outlining the principal features of the case which lately came under my care, it will be seen that it is a typical example of the disease, and differs in no essential detail from the average case reported in the literature on the subject. The labour was somewhat tedious, by reason of a persistent occipito-posterior presentation in a primipara, and forceps were required to effect delivery. How far these facts support the theory of harmful pressure upon internal organs, or of a central nervous system lesion as a cause of the hæmorrhage, will never be known any more than has been alleged in the few cases reported. The child was fairly large, and, contrary to the rule, was a girl. Without any doubt, pressure greater than normal was experienced by the infant. In every way the child appeared normal at birth; there was a caput and moulding of the head, but no hæmatoma.

The day following its birth, the child vomited a little bright red blood with smallish clots at intervals, and the stools showed both black and red blood in quantity. The third day, blood was copious by vomit and

motions, and the child's condition was becoming grave as a result. The mother's breasts were pumped, and the child spoon-fed with the milk. The child was with difficulty kept warm with the aid of wool and artificial heat, and was failing rapidly. I gave a gloomy prognosis, and obtained permission from the parents to adopt any treatment which I thought might be of use.

The urgency of the case, and, being a Sunday, the added difficulty of getting and sterilizing gelatin, prompted me to think that horse serum by injection would hold out a hope as great as, if not greater than, that to be anticipated from the use of gelatin. I was willing to use anti-diphtheritic serum, if I failed to obtain the plain variety, believing that the diphtheria element would be harmless even if no value. However, I was fortunate enough to obtain the plain horse serum in a 10 cc. phial.

With fullest precautions, I injected 5 cc. under the right axilla, about the horizontal nipple-line, and with the fear of not being able to obtain more serum, should I require it next day, and of possible anaphylaxis resulting from a second dose, together with the difficulty of keeping sterile the 5 ccs. remaining in the flask, I determined to give an heroic dose, and promptly injected the second 5 cc. under the left axilla. The punctures were duly sealed with care. I should have said that, for 24 hours prior to this, the infant had been given 2 mins. of adrenalin solution, every two waking hours.

The following day, no blood whatever was vomited, the child took more nourishment and seemed a little stronger. There was still marked melæna, but no red blood by the bowel. On the sixth day, there was no blood of any sort coming by vomit or by bowel. On the seventh day, some tarry blood was visible in the motions, but still some of the latter was normal in colour. That was the last blood seen. From thenceforward the child progressed favourably and rapidly, considering its grave condition on the third and fourth days, and is now a normal healthy infant.

I would also like to allude to the fact that Glendinning has shown that a *minute* quantity of blood may be a *normal constituent* of infant fæces during the first few days of life. It is considered by him to be caused by the sudden circulatory changes following an independent existence, which lead to minute hæmorrhages into the intestinal canal. It has been suggested that too early ligation of the cord may be a factor in the case, but investigation of this point has not confirmed the theory.

With regard to the serum injection, I am not aware of any previous instance of its use in such a case, although Dr. Müller, of Tubingen, has used *human* serum with success in cases of infantile eczema. I am forced, in spite of the single instance, to the conclusion that the favourable and rapid result was directly attributable to the serum injection.

Practical Notes.

TREATMENT OF ANAL FISSURES.

These may often be treated successfully by correcting the constipation, and applying antiseptics to the fissure. The latter may be obtained by the use of one of the following ointments:—

(1) ℞ Unguenti Styracis,
Balsami Peruviani - - - - ana ʒij.
Misce. Fiat unguentum.

(2) ℞ Collargol - - - - - gr. xxx.
Iodol - - - - - - gr. xv.
Stovain - - - - - - gr. iss.
"Baume du Commandeur" - - - ʒiiss.
Paraffini Liquidi - - - - - ʒv.
Misce. Fiat unguentum.

(3) ℞ Extracti Krameriæ - - - - - gr. xlv.
Balsami Peruviani - - - - - ʒi.
Olei Amygdalæ dulcis - - - - ʒv.
Misce. Fiat unguentum.

(4) ℞ Collargol - - - - - - gr. xxx.
Paraffini mollis - - - - - ʒiij.
Misce. Fiat unguentum.

Immediately after passing a motion, the patient must make a careful *toilette*. He then places on the edge of the anus a small piece of the ointment, and gently insinuates this through the anal orifice. If these measures prove unsuccessful, the application of tincture of iodine should be tried before resorting to dilatation of the sphincter.—(*Journ. de Méd. et de Chir. prat.*, October 10, 1914.)

TREATMENT OF SEPTIC WOUNDS WITH TURPENTINE.

At a recent meeting of the *Société de Médecine de Paris*, Lematte described a new method of treatment for septic wounds. Trials were made of various essences, but more particularly with turpentine, because of its recognized leucocytogenous properties. The experience, based upon several hundreds of cases, has shown that the following technique gives the best results. The ideal in view was a combination of antiseptic properties without toxic effect on healthy tissues.

The following solutions are employed:—

Solution A:—
Fuchsine - - - - - - gr. ½.
Turpentine
Alcohol (95°)
Ether - - - - - of each 2½ drachms.
Mix.

Chemically pure turpentine is of no use, and must not be used in this

preparation.

Solution B :—

Sodium Chloride - - - - -	2 drachms.
Triturate in a mortar and add—	
Turpentine - - - - - -	25 minims.
Then add by degrees—	
Boiled water - - - - -	35 ounces.

This mixture must be shaken up for some hours, and then filtered to remove the small excess of turpentine.

Method of Using :—The wound, such as one caused by a bursting shell and soiled with *débris* of various kinds, is first treated for 15 minutes with a compress soaked in undiluted 12-volume hydrogen peroxide solution. It is then washed with a lotion composed of equal parts of 12-volume peroxide of hydrogen solution and solution B, and carefully dried with swabs of sterilized gauze. All dead tissue is removed with forceps and scissors.

Solution A is then applied freely to the wound by means of absorbent wool swabs, or better still a camel's hair brush. The solution must be rubbed thoroughly into all parts of the wound. All the infected tissues become vivid red in colour. After being allowed to dry for a few minutes, the wound is covered up with a compress and a layer of sterile wool, soaked in solution B, and kept in place by a bandage. No oiled-silk or its substitutes must be used.

The dressing is renewed every day. On the first day after the application, the wound shows the healthy tissues full of blood, the infected parts of a pale rose tint, and the necrosed parts of a violet-red colour. It is washed with solution B and dried. Solution A is only applied when any part has a pale rose colour. Suppuration disappears after the third or fourth dressing, and a healthy granulating surface is obtained. Healing takes place quickly and well, more so than with iodine. If exuberant granulations appear, these are touched with solution A. Fistulous wounds are packed with gauze soaked in solution A. Stains on healthy skin and on linen are soon effaced.—(*Bull. et Mém. de la Soc. de Méd. de Paris*, *No.* 1, 1915.)

TREATMENT OF TYPHOID FEVER BY APPLICATION OF ICE TO THE ABDOMEN.

From being a convinced advocate of the cold-bath treatment of typhoid fever, de Massary has come, after some years' experience, to look upon them as useless if not harmful. Tepid baths and wet packs are equally condemned by him. He now pins his faith to the permanent application of a large ice-bag to the abdomen, from the beginning of the disease until the stage of complete apyrexia is attained. He attributes to this continuous cooling of all the abdominal organs the excellent results he has achieved for some time past. These are a very low rate of mortality, a progressive and usually quick fall of the temperature, and the rare appearance of relapses and of complications. He is inclined to connect hæmorrhages with the cold-bath treatment, and does not now accept the teaching of Trousseau that these losses of blood benefit the patient, and are "phenomena of

favourable augury."

His method of procedure is simple and easily carried out, and has been adopted in several of the French hospitals recently. When the patient, as a rule a soldier from the trenches, is admitted, he is carefully cleaned by being kept in a hot bath (36°–37° C.) for 20 minutes, plenty of soap being used. As soon as he has been put to bed, the surface of the abdomen is covered with a thick layer of powdered talc, and over this is spread a piece of thin flannel. On this is placed a large-sized rubber ice-bag filled with large pieces of ice. Care is taken that the ice-bag lies as flatly applied as possible, by leaving as little air in it as can be managed before screwing on the cap. The whole is kept in place by a folded draw-sheet, which is preferable to a bandage for that tends to roll up into a cord and allows the ice-bag to fall out. The talc protects the skin completely from injury, and the flannel used must not be thick, or it will not allow the cold to penetrate. The ice dissolves in about two hours and a half, when the bag must be refilled with ice. This does not disturb the patient in the least, no moving being required.

In this way, the second important detail of treatment is ensured, that is, absolute rest. This is even more important for soldiers than for civilians, for the soldier arrives at the hospital completely knocked-up, and rest alone would be the best treatment for him.

The third matter of importance in the treatment is to give the patient an abundance of fluids. The amount should reach as soon as possible from 4 to 5 litres in the 24 hours, and is made up of milk (2 to 3 litres) "laced" with coffee, tea, or rum, barley-water, orangeade and lemonade. The mouth must be cleaned out carefully after each feed; the free use of fluids keeps it moist, and thus averts the suppurative parotiditis which is sometimes met with in soldiers from the front, who have been without drink for a few days. The kidneys are kept acting freely, and when the amount of urine passed is from 5 to 6 litres, convalescence is close at hand.

If the patient is unable to take fluids freely by the mouth, he should be given large enemata of boiled water containing 50 g. of sugar to the litre. The enema must be given very slowly to allow the fluid to be absorbed; one litre takes between four and five hours for absorption. If enemata are rejected or not tolerated, they must be replaced by hypodermoclysis or intravenous injection of normal saline with glucose. As a rule, the patient is able after a few days to take the full quantity by the mouth.

The application of the ice is kept up until the temperature has fallen to normal, and remained there for two days. Solid food is not given until the temperature has remained normal for six days. De Massary, in conclusion, points out that only by his method is it possible to treat a large number of typhoid cases at the same time, for under such circumstances the bath treatment could not be carried out.—(*Presse médicale*, No. 2, 14.)

Reviews of Books.

The Ileo-cæcal Valve. By A. H. Rutherford, M.D. Pp. 63 and vii. Two coloured plates, 20 half-tone plates. London: H. K. Lewis. 6s. net.

The book consists of two parts: Part I. dealing with the literature on the subject; Part II. with the author's account of his own observations and experiments.

Part I.—According to the observations of authorities mentioned, there appears to be no definite type of valve. Its action is considered to be chiefly mechanical, the flaps acting in a similar manner to those of the valves of the heart. These authorities seem to incline to the view that the valve is competent during life, and that the oblique entry of the ileum into the cæcum is of the utmost importance.

Part II.—The author describes a living specimen—observations being made through a cæcal fistula—and also 32 specimens in detail prepared by immersing in 10 per cent. formalin immediately on removal from the body soon after death. Dried distended specimens are considered of little value.

The observations on the living specimen seem by far the most important, and seek to establish the fact that the valve during life appears in the cæcum as a smooth, red, cherry-like protrusion, usually covered by the mucous membrane of the cæcum. During peristalsis, this button becomes more prominent towards the cæcum and ejects fluid fæces. A probe can only with difficulty be passed through the valve, but under deep chloroform anæsthesia one finger and sometimes two may be passed into the ileum, thus tending to show that there is some muscular sphincteric action of the valve.

Another interesting point elicited is, that stimulation of the cæcum by enema, or by douching the mucous membrane of the cæcum with warm water, excites peristalsis in the small intestine.

The work inclines to show that the action of the valve is sphincteric, similar to that of the pylorus, and that the musculature is derived from the circular muscle of the ileum, and partly from the deepest layers of the longitudinal coat. The mechanical action of the valve is of quite secondary importance to the sphincteric.

The thesis is accompanied by a useful bibliography, and 20 excellent half tone plates of formalin specimens.

It can be recommended as an interesting monograph on the subject.

Cunningham's Manual of Practical Anatomy. Revised and edited by Professor Arthur Robinson. Sixth edition. Vol. I. With many illustrations and plates, of which some are coloured. Pp. 650. London: Oxford Medical Publications. 10s. 6d. net.

Cunningham's *Manual of Practical Anatomy* is so well known and so deservedly popular, that to review this new edition is chiefly to com-

pare it with its predecessors. As in the last edition, the International B.N.A. terminology is used, but happily in most cases the old terms are given in brackets, and a glossary showing new and old terms opposite each other is put at the beginning of the book.

The scheme of the work is, as before, essentially a companion in the dissecting room, the whole subject being treated in areas convenient for dissection. The descriptions of the anatomical parts are wonderfully accurate and clear, and with the aid of the magnificent illustrations afford the modern student facilities for learning anatomy, under conditions so greatly improved, as to excite the envy of old stagers. Among these we would call attention to the illustrations showing cutaneous nerve supply, muscular attachments, ligaments and articular surfaces, transverse sections through limbs at various levels, and through joints in such directions as to show the relations of synovial membrane and of other structures outside the joint. Very great improvement has been made in a large number of illustrations, particularly in those of the abdominal viscera and other structures in position. These are now enlarged to occupy a whole page and the details are far more clearly seen.

A valuable collection of radiograms, showing the normal condition of the bones and joints, and the abdominal viscera after administration of bismuth meals, is reproduced at the end of the book, and will prove extremely useful to the student and young surgeon, enabling him to become familiar with the normal appearances of the parts shown by the X-rays, and so by comparison assisting him to detect evidences of pathological change.

The Pharmacopœia of the Hospital for Diseases of the Throat, Nose, and Ear (Golden Square). Edited by C. A. PARKER, F.R.C.S., and T. JEFFERSON TAULDER, M.B., B.C., F.R.C.S. Pp. 62. Seventh Edition. London: J. and A. Churchill. 2s. 6d. net.

THIS, the seventh edition of the Throat Hospital Pharmacopœia, is its Jubilee edition, since it is now 50 years since the hospital was founded. A study of this, in comparison with the previous editions, is interesting as showing the evolution of nose, throat, and ear therapeutics. It has been arranged in alphabetical order to render an index unnecessary. Formulæ which have become obsolete or redundant have been omitted, and amongst notable additions are Capsules, Fomentations, Peroxide of Hydrogen, Formalin, and Adrenalin. The book is a most useful addition to therapeutic formulæ.

The Newer Physiology in Surgical and General Practice. By A. RENDLE SHORT, M.D., B.S. Third edition. Pp. xii. + 256. Bristol: John Wright and Sons, Ltd. 5s. net.

THE scope of this new edition of what is now a well-known work has been much increased. Additional chapters on the vitamines and the genital glands have been introduced, and those on surgical shock, the pituitary and pineal glands, and digestion have practically been rewritten. The ductless glands have assumed such importance nowadays that much new matter respecting the thyroid has necessarily been introduced. The chapter on

surgical shock is excellent, and the various hypotheses are admirably stated. For the general practitioner who desires to keep himself abreast of modern research, the book is indispensable, and he will find in it a multitude of hints to aid him in the treatment of disease. The author's practical acquaintance with his subject is evinced by the numerous experimental investigations, which he himself has contributed to the subjects with which he deals. We anticipate that this new edition will be as widely read as its predecessors.

A System of Clinical Medicine. By Thomas Dixon Savill, M.D. Pp. 948, 4 plates in colour, 170 woodcuts. Fourth edition. London: Edward Arnold. 25s. net.

In October 1912 we reviewed the third edition of this work, and the high opinion we then formed of it has evidently been shared by the profession, for another edition has been called for in the space of two years.

Special attention is directed in the preface to the re-casting and complete revision of the chapter on diseases of the heart, and we can testify to the ability with which this has been carried out. The chapter gives an admirable account of the modern methods of investigating diseases of the heart. In the account of the general symptoms of mitral stenosis it is stated that 'Liver enlargement and ascites are more common, and dropsy of the extremities less common, in mitral stenosis than in mitral regurgitation." This is quite in accordance with our own observation, but we do not remember to have seen this fact so clearly stated in other text-books. In the chapter on aneurysm of the aorta, hardly sufficient stress seems to be laid upon the importance of an X-ray examination, but it may be stated confidently that in some cases a correct diagnosis is only possible by this means.

Fifty-three pages are allotted to diseases of the skin. It is impossible in this limited amount of space to give anything like an adequate account of cutaneous affections, and we are of opinion that it is not desirable to include this department in a text-book on general medicine. The last chapter is devoted to "Examination of Pathological Fluids and Clinical Bacteriology," and gives concise, but clear and very practical directions for the methods of obtaining various pathological fluids and how to examine them.

With even more emphasis than when we reviewed the third edition, we can recommend the present volume to our readers.

Lunacy Practice. By W. H. Gattie, Barrister-at-Law. Pp. 59. London: Shaw and Sons. 2s. 6d. net.

The aim of the author of this short manual is to set forth the formalities necessary for the reception of patients into institutions for the insane, and to give as concisely as possible useful information relative to the Lunacy Acts. It is a compilation of all the various forms and certificates required under the Acts; it shows the manner in which these should be filled in; and it gives short notes concerning the chief legal points with which the practitioner may be called upon to deal. We have no doubt that it will prove of use to medical men. Unfortunately, it was published before the passing of—and therefore gives no account of that most important piece of recent legislation—the Mental Deficiency Act. Doubtless this will be remedied in a subsequent edition.

THE PRACTITIONER.

JUNE, 1915.

INSUFFICIENCY OF QUADRICEPS.

By JOSEPH E. ADAMS, M.S., F.R.C.S.

Surgeon in Charge of Out-Patients to St. Thomas's Hospital, etc.

THE wasting of muscles, which act on any given joint, is a well-known accompaniment of disease affecting the movements of that joint, but I think it is hardly realized that the muscular wasting, as a pathological lesion, may outlive the articular changes, so that although the joint surfaces become normal again, the function may not be restored for many months. For the perfection of its mechanism, a joint depends on the structures of which it is composed: bone, cartilage, capsular ligaments, synovial membrane, in some cases intra-articular fibro-cartilages, the muscles which move it, and the nerves which supply them. Any affection of these component parts, whether traumatic, inflammatory, degenerative, or neoplastic, is liable to upset the co-ordination of movements and sensations, which enable a joint to carry out its allotted functions. In whatever way this inability arises, it inevitably reacts upon the muscles, for muscles which do not perform their normal amount of work become weakened and atrophic. In no lesion is this muscular wasting more noticeable than in that form of tuberculous arthritis known as *caries sicca*. The explanation of this is, that the first movement to be limited by reason of its painfulness is abduction, and the most casual observer is able to note the difference in contour of the deltoid on the two sides of the body. But it is especially in reference to the knee-joint and its muscular system that I propose to call attention, and to show how the normal functions of the knee-joint depend on the condition of these muscles.

FUNCTIONAL EFFICIENCY OF JOINTS.

For perfect function, it is essential that a normal joint should have healthy muscles around it. It is obvious that

a damaged or diseased knee cannot work satisfactorily, even with perfect muscles; it is less obvious, but none the less true, that a perfect joint cannot continue its function normally with weakened or atrophied muscles. In other words, the peri-articular tendons and their muscular bellies must be included in the list of structures given above, on which the functional value of a joint depends. The more complicated the articular structure, the more it is dependent on the integrity of all its parts.

WASTING OF THE THIGH MUSCLES.

A shrunken condition of the thigh muscles is a well-known feature of old standing disease of the hip or knee, but it is present as well in cases of temporary disability of these joints, and I propose to consider this wasting with especial reference to injuries of the knee, whether recent or remote. The most important conditions that demand consideration are traumatic synovitis and internal derangement of the knee-joint, and the inter-relationship between these injuries and the condition of the muscles is very marked. It may be regarded as almost inevitable that, if the knee-joint is put out of action for as much as a week, retrogressive changes take place in the thigh muscles, and, in my experience, these are more marked in the anterior extensor group than in the hamstrings. It is therefore necessary in examining all cases of injury of the knee, and in the slighter degrees of inflammation, to pay attention to the condition of the muscles as well as that of the joint itself. One of my reasons for laying stress on these points is that I have recently had several cases sent to me labelled "internal derangement of the knee-joint," in which the local condition and the after history of the case have proved that the knee-joint was normal but the muscles controlling it were deficient in power, and thus the joint was weak and unreliable; in some instances even, there was a definite history of the joint "giving way" and letting the patient down.

EXAMINATION OF THE KNEE.

Putting aside examples of tuberculous and other forms of chronic or sub-acute arthritis, in which the eye can detect gross changes and there is obvious limitation of movement, it is important to have a definite standard by which the func-

tional condition of a joint can be estimated. A healthy knee exhibits—

(*a*) Extension up to an angle of 180°, *i.e.*, until the leg is in the same line as the thigh.

(*b*) Flexion so that the calf comes in contact with the posterior surface of the thigh.

(*c*) No lateral mobility when the leg is in a position of complete extension.

(*d*) Some degree of rotation when the leg is flexed at a right angle.

(*e*) No lateral mobility of the patella when the quadriceps extensor is strongly contracted.

(*f*) The hardness of the quadriceps, especially the vastus internus fibres, should be equal on the two sides.

(*g*) The circumference of the thighs at a fixed point, say four inches above the upper border of the patella, should be equal on the two sides.

If these requirements can all be met, it is practically certain that the knee is sound, but if any one of them exhibits deficiency the functional value of the joint will be impaired, and the knee may easily be blamed on account of the insufficiency of the quadriceps. In referring to the movements above mentioned, I mean passive movements; active movement may, of course, be limited purely by the lack of muscular power.

INSUFFICIENCY OF QUADRICEPS AS A CLINICAL ENTITY.

If, then, the function of a knee-joint is seriously impaired owing to muscular weakness, especially of the quadriceps extensor, it is important to recognize the true nature of the lesion and how it arises. In the first place, it must be recognized that the complete action of a muscle can only be executed if the joint which it acts on is free to move, and if the contraction of the muscle does not cause pain. If a muscle is bruised, activity of that muscle is interfered with by involuntary inhibition, and if the condition persists, wasting is bound to become manifest. Even if the patient fights against it, the muscle will not contract to its full if the act is painful. A similar inhibition occurs in the case of injuries to joints, for movement is usually painful and therefore it is reflexly avoided.

Of all the doctrines ever preached, that of Hilton's, that

pain demands treatment by rest, is one which has, in my opinion, been sadly misapplied in the case of joint injuries. In the first place, it is by no means certain that the principle is correct, and it is quite certain that the practice is not, if rest is to be used until all the pain has gone. The over-application of this principle of rest for the treatment of pain has done much to build up the reputation of the bone-setter at the expense of the medical practitioner. Let us consider what frequently happens in the case of what is termed "traumatic synovitis of knee." This leads to rapid effusion into the joint and impairment of its powers from the presence of the excess of fluid and on account of the pain due to distension of the capsule; in the majority of cases, there is no evidence of rupture of ligaments or displacement of any intra-articular structures.

The common method of treatment is rest and hot fomentations, or possibly cold applications; the rest to the joint is often secured by the use of a back splint. This treatment in the earlier stages is followed later by further rest and massage, with perhaps some exercises against resistance, and the application of a pressure bandage over the knee. The main principle of this method of treatment is rest, until the excess of fluid has been absorbed from the joint, but it is very doubtful how far such rest actually favours the absorption of fluid, and its part appears to be rather in the direction of preventing fresh outpouring of synovial fluid. Meanwhile, the muscles waste, and the degree to which this occurs may be estimated when I state that, in a number of cases, I have found that, within a week of the onset of effusion, a loss of half-an-inch in the circumference of the affected leg is quite common.

Under this *régime* it is rare for the patient to be able to use the joint in less than three weeks, and then he usually finds it is necessary to walk with a stick for a further period, so that full restoration of function is not obtained for about six weeks from the date of the accident. The use of massage to the muscles of the thigh and leg may hasten the recovery of power over the joint, but frequently fluid is present for many weeks and there is a feeling of weakness in the leg. The longer the period of rest, the less security there is in

the joint, and the stronger the tendency to recurrent effusion when strain is put upon the joint. The explanation of this lies in the fact that as long as there is an excess of fluid in the joint the quadriceps is unable to contract to the full, and weakness of the quadriceps leads to laxity of the capsule of the knee, and therefore favours the accumulation of fluid within the joint. In my own experience, after using most of the recognized methods to hasten absorption of fluid from the knee-joint, I have found that ionization, for periods as long as from half-an-hour to forty minutes, is the most effectual. Chlorine ions are in most cases all that is necessary, and the treatment may be applied on alternate days without interfering with the use of the limb. The application of an elastic bandage to produce constant pressure over the knee is helpful, and this should be worn for the first few days to walk about in. No enforced rest for the joint is necessary. This treatment can easily be combined with the electrical stimulation of muscle discussed in the succeeding paragraph.

THE QUADRICEPS IN RELATION TO INTERNAL DERANGEMENT OF THE KNEE-JOINT.

This term is often used to include displacement of semi-lunar cartilages, nipping of synovial fringes, loose bodies, etc. All these conditions impair the functions of the joint in some degree; secondary atrophy of muscles takes place at an astonishing rate, and as long as the derangement persists, it is impossible for the normal tone of the muscles to be regained. This condition is exactly parallel with that which obtains in tuberculous arthritis, but it is not generally recognized that, even after the derangement has been treated successfully by manipulation, the muscular atrophy may persist and become almost permanent. It is probable that the liability to recurrence in cases of displaced semi-lunar cartilage, properly reduced and carefully treated after the first mishap, is due mainly to the persistent weakness of the quadriceps.

Consideration of some points in connection with displaced cartilage will serve to illustrate the relationship of the quadriceps to the functional working of the knee-joint. The line of treatment commonly adopted is, in the first place, reduction

under anæsthesia if necessary; when successfully performed the cartilage slips back into its place with an audible click, and the movements of the joint are restored.

It is usual then to immobilize the joint on a back splint, or in a plaster of Paris case for some weeks. At the end of this time massage, together with gentle movements, is permitted, and by degrees the patient is allowed to use the leg, though warned against any violent exercise for months afterwards. It may be admitted that in some cases the result is excellent; in others, the knee can be used for ordinary walking, but remains for months, and even years, inferior to the other one. In yet other cases, recurrence of the displacement occurs, and, if this happens frequently, the surgeon is consulted with a view to the removal of the displaced cartilage. It is then necessary for him to decide as far as possible from the details of the history whether it is clear that the cartilage has been displaced, and, secondly, whether it is out of its place when he examines the patient. The second question is the easier one to decide, for, if the cartilage is occupying an abnormal position or is torn, there is usually impairment of movement or local thickening in the position of the anterior end of the cartilage. Displacement of the cartilage is usually inwards towards the centre of the joint, and thus an abnormal gap may be felt.

As regards movement, this may be limited in any special direction having relation to the nature of the displacement; a good criterion is afforded by asking the patient to squat down on his heels; if this can be done without assistance it is pretty certain that the cartilage is not seriously displaced. If this test is passed, there may still be a clear history of a displacement requiring forcible reduction, or of frequent occasions when the joint has given way or been "put out," and when there is a definite history of locking of the joint and recurrent effusion, it is probable that there is detachment of part of the cartilage. However, there are numerous cases in which the cartilage has been put out and weakness of the knee has persisted, and a larger number still in which no actual injury of this sort has occurred, but the knee is unreliable, and frequently feels as if it might give way. All these cases must be carefully investigated according to the principles laid down above, and after the movements of the knee-joint have

been investigated, the thigh muscles must receive special attention. Where the knee passes muster, it may frequently be found that the fault lies in the quadriceps; measurement of the thigh will show atrophy of muscle, and comparison of the hardening of muscle fibres on contraction, particularly those of the vastus internus, will show obvious inferiority on the affected side. Examination of a series of cases of this sort will reveal three types at least, viz.:—

(1) Those in which a diagnosis of internal derangement, probably due to damaged or displaced cartilage, is quite clear.

(2) Those in which a displacement has probably occurred, but it has not been repeated, but only threatened owing to persistent muscular weakness.

(3) Those in which a slight injury to the joint, not causing serious disability, has led to chronic weakness and insecurity owing to muscular atrophy.

In addition, one must recognize that all cases of true internal derangement have accompanying insufficiency of quadriceps.

SELECTION OF CASES FOR TREATMENT.

Displaced or torn cartilages require removal, and cases of one certain displacement followed by recurrences usually require operation; insufficiency of quadriceps does not require operative interference, for, if only the muscles can be brought to a state of normal efficiency, the insecurity of the joint will become a thing of the past. Inasmuch, however, as insufficiency of quadriceps is a common factor in several types of case requiring operation, it must not be thought that operation concludes the treatment of the lesion.

It may perhaps be well to give in detail the after-treatment in the case of operations for removal of displaced and torn cartilages, which I have recently adopted in co-operation with Mr. W. R. Bristow, who is in charge of one branch of the electro-therapeutical department at St. Thomas's Hospital, but now serving with His Majesty's Forces. For details of his method of electrical stimulation of the muscles, I would refer the reader to an article published in the *Lancet* of May 4th, 1912, by Smart and Bristow. Concerning the details of operation, suffice it to say that I endeavour to remove the whole of the cartilage, and close the joint with a

few silk sutures for the synovial membrane, and firm suturing of the capsule, also with silk; the skin is closed with salmon gut, and the knee firmly bandaged in a voluminous dressing without any splint. The wound is examined on the fifth day, and a collodion dressing applied; the knee is covered with an elastic pressure bandage, and the patient allowed up. From this day electric stimulation of the muscles is begun, and continued daily for gradually increasing periods. On the eighth day, walking is permitted, and at the end of a fortnight the joint can be moved freely, walking is perfect, and there is very little effusion. The pressure bandage is used for walking always in the first two weeks. At the end of this time it can be discarded, and all forms of exercise can be indulged in; if the muscles were not greatly wasted before the operation, they will then probably have returned to their full standard of efficiency. The average length of time for complete cure, with no weakness of joint and no liability of effusion, in a series of cases treated on these lines was 20 days. Without these steps effusion into the joint is apt to occur after the operation, as soon as the patient walks about, and often persists for a couple of months. Although the presence of the fluid is not serious, it prevents the proper action of the quadriceps, and perfect recovery is not possible until the fluid is absorbed.

Similar operative procedure is required in cases in which recurrent displacement occurs, but it is not necessary to explore the joint, unless there is a moral certainty that displacement of cartilage has occurred or that some other lesion is present requiring removal, such as a thickened synovial fringe or loose body. In doubtful cases, then, it is clear that all the less severe symptoms of internal derangement of the knee may be due to insufficiency of the quadriceps, and that these cases must be distinguished from those for which arthrotomy is required. One sees a large number of cases labelled "internal derangement of the knee," in which a slight injury to the joint has been followed by muscular weakness; treatment of these on sound electrical lines will effect a cure in 100 per cent. of cases.

A word must be said of massage, and, from my own experience, I would state that in inducing absorption

of fluid in the joint massage is disappointing, and in developing wasted muscle appallingly slow, so that electrical methods can do in days what massage takes weeks to perform. The explanation of muscular atrophy, as an almost universal accompaniment of the many injuries and disabilities of a joint, is that it is a physical impossibility for a muscle to go on doing its full work, if the action causes pain to the patient; involuntarily, the muscle is spared, and the patient stops short of movements which are painful. Electricity compels the muscle to contract from a minimum up to its maximum, and it is the method of graduated contraction which enables the muscle to be developed with little or no pain until actual hyperplasia results. Thus, a wasted muscle acting on a healthy joint can be developed, until it is equal to, or even stronger than, one which has never fallen below its normal degree of tonicity and power.

I may have laboured these points somewhat, but I have been impressed by the number of cases in a large Hospital Out-Patient Department, in which the only lesion actually present is insufficiency of the quadriceps. They are commonly sent up as cases of internal derangement, chronic effusion, loose body, etc. Recently, I have come across several such cases in young soldiers over-strained by route-marching, in which a previous slight injury to the joint is stated to have occurred before the war, and the extra work demanded of the ambulatory system has found out the chronic weakness of the quadriceps extensor. A few weeks' electrical treatment has restored to efficiency several men who would otherwise have been discharged as unfit.

HEART PERFUSION WITH ALCOHOL.

By D. T. HARRY, M.D., F.R.C.S., etc

Professor of Physiology, University College, Cork, etc.

Perfusion of the heart with alcohol has not been extensively tried, but in so far as it has been investigated, the results, especially when compared with those of simply dropping alcohol on the heart, are somewhat anomalous. In hearts of similar type and condition, however, it must be said they are fairly consistent.

It has not been made clear how alcohol affects the various factors in the nerve-complex of the cardiac mechanism at different stages of its action, in comparatively weak concentration. In the present research, attention has been devoted to this aspect of the question in the toad's heart.

The method adopted was similar to that described by Mines.[1] The cannula is tied into the inferior vena cava below the liver, an operation which requires some little care. The aortæ are cut across, and if it be desired to pass the fluid through more rapidly than from 1·5 to 2 cc. per minute the auricle must be slit. The alcohol is mixed with Ringer's solution, and in small percentages the perfusion mixture is nearly isotonic with the tissues. In the records, the auricle tracing is the upper one.

According to Pembrey and Phillips,[2] alcohol in strong doses causes loss of power of rhythm and automatic properties, but not paralysis of the muscle. These observers used the method of dropping alcohol on the heart. They say that it diminishes frequency and increases force. Perfusion gives somewhat different results from these.

Grützner[3] showed that minute amounts have a stimulating action, which was, however, temporary, and nearly always succeeded by a deleterious effect. Dold[4] showed that the toxic action of alcohols increased the higher in the series one went, the effect of amyl alcohol being extremely deleterious even in the minutest amounts.

A 2·5 per cent. solution of ethyl alcohol in Ringer's solution is shown to cause a gradual diminution in force and rate of the auricle, while the ventricle is diminished in rate only, and the heart recovers spontaneously on shutting off the drug. The record (Fig. 1) shows the effect of 5 per cent. alcohol in Ringer's fluid. Again, the auricle fades off more quickly than the ventricle, both chambers ultimately coming to a full stop. Perfusion with Ringer's solution was begun a few seconds later, and continued to the end of the record. During several minutes the heart remained quiescent, and numerous stimuli, indicated by the marks on the base line, applied to the heart muscle during the greater part of this interval, showed irritability or contractility lost (muscle paralysis). Later on, single stimuli gave rise to single contractions, and finally a single stimulus started a continuous rhythmic beat with the ventricle showing a little initial tonus.

Dold asks if alcohol affects muscle or nerve. It affects both. In the record (Fig. 2, page 786) a weak stimulation of the crescent (first signal mark) is seen to cause a pure acceleration. A 2·5 per cent. solution of alcohol is then used to perfuse; the heart is slowed, and the same crescent stimulus gives no acceleration, but almost immediate arrest.

The accelerator nerves have been paralysed before the inhibitors. Recovery takes place by washing out with Ringer's fluid, as shown by the third stimulus, which again causes acceleration. It is difficult to show

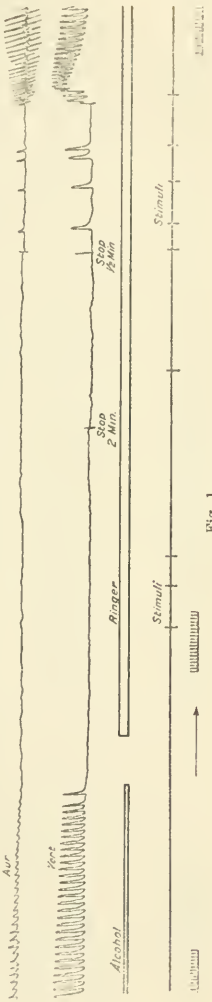

Fig. 1.

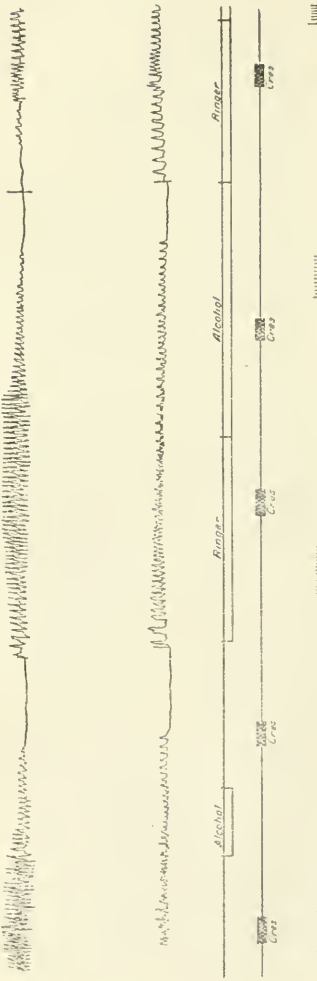

Fig. 2.

paralysis of the inhibitor nerves, for the heart is generally stopped by the time it is complete, but a glance at the result of the fourth stimulation in the figure shows that the inhibitor effect is delayed. In the next record (Fig. 3, page 787), it will be seen that crescent stimulation, at a period when alcohol has slowed the heart, gives neither acceleration nor inhibition (one extra beat occurs, but the rate is recovered under the influence of Ringer's fluid). After long washing with Ringer's fluid, the same stimulus gives slowing and arrest. Why the auricle in this case does not recover *pari passu* with the ventricle, it is difficult to say, unless it be due to depression of accelerator auricular nerves, or a greater sensibility of auricular muscle. The mechanical effect of perfusion may mask the action of the poison on the ventricle.

The heart recovers by evaporation of the volatile poison, and is greatly aided by perfusion with Ringer's solution. It may be said that in certain

cases, which would not recover spontaneously, Ringer's fluid effects recovery. The importance of perfusion for recovery of muscle irritability and conductivity may be shown in another way; both auricle and ventricle are stopped by alcohol, and a clamp is placed in the a.v. groove with merely sufficient pressure to stop the perfusing fluid from reaching the ventricle. The auricles are now set going with Ringer perfusion, while the ventricle, bathed with the fluid from the outside, remains quiescent. On loosing the clamp while the perfusion fluid is turned off, there is no change, but on again turning on the solution, recovery is slowly established in the ventricle.

It may be shown that small amounts of alcohol augment the frog's heart, and an augmentor effect, too, in the case of man has been described. Grützner thought the increased conductivity of the heart after a small dose was due to nerve stimulation. Some believe that the increased pulse-rate is not due to alcohol itself so much as to the situation in which it is drunk, atmospheric and exciting conditions exaggerating it.

Like other accelerator depressants, alcohol has an initial stimulating effect on those nerves, but it is quite transitory and only seen with weak solutions. It is probable that inhibitor paralysis, or partial paralysis, in the intact heart is to a certain extent, the cause of increased rate, but this connotes an interference with nerve control, which can only have a deleterious effect ultimately.

When the heart is stopped by

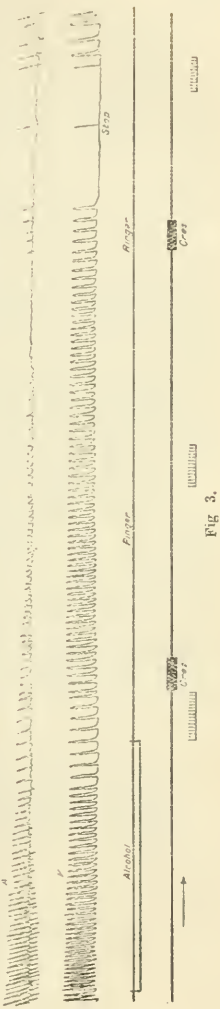

Fig. 3.

alcohol, both chambers generally cease together, though the weakening effect is more marked on the auricle.

Pembrey and Phillips state that alcohol does not cause paralysis of the heart muscle, and describe no stage of arrest where artificial stimuli do not give muscle responses. As shown in Fig. 1, complete paralysis lasting for more than two minutes has been caused by perfusion with 5 per cent. solution. Irritability and contractility are completely lost, but recovered by perfusion with Ringer's solution.

The first effect of alcohol in weak solution may be excitation of accelerator nerves, which, however, quickly undergo depression under its influence. During this depression of accelerator nerves the rate of beat may or may not be slowed, and the inhibitor nerves in this phase are intact as shown by complete arrest of beat on stimulation.

Stronger solutions, when perfused, bring about cessation of beat—loss of rhythm without paralysis, as described by Pembrey and Phillips for outward application of the drug—which on continued perfusion passes into complete paralysis.

The irritability of the muscle, the last property to go, is recovered independently of the rhythmic power which comes later. Are we to look on these properties of muscle as recovered under the influence of perfusion independently of nerve action? We have clear evidence that nerves are early affected, and it may be that muscle has a limited capacity for independent rhythmic action, which recovers only secondarily to nerve recovery. This does not necessarily connote rhythmic nerve centres in the heart itself.

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THE TREATMENT OF NASAL ACCESSORY SINUS DISEASE.

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On a former occasion,* I dealt with the diagnosis of nasal accessory sinus disease. I now propose to consider, in a general way, the treatment, without going minutely into the details of operative procedures.

There can be no doubt that nasal accessory sinus disease is more common in countries where the climate is cold and damp. In saying this, one does not deny the position of dental caries in the causation of maxillary antral disease. Even in this, however, the larger proportion of cases arises from infection by way of the nose and not by way of the alveolus. Moreover, most cases of accessory sinusitis do not begin acutely, they are chronic from the beginning. Again, though influenza, scarlet fever, and other infectious fevers may be incriminated as causes in some cases, in frequent cases no doubt, in the larger number no such history can be obtained.

The commonest history is one of recurring colds in the head, at first during the winter months, and then at other periods of the year, till finally the cold in the head is continuous. By this time sinus disease is in many cases already established. Indeed, if, as we should, we regard the lining membrane of the various accessory spaces as continuous with that of the nose itself, it would hardly be possible to say at what period the catarrhal condition spreads from the latter into the former. It follows as well from this that as nasal catarrh itself shows seasonal variations, so does accessory sinus disease in the early stages. This has frequently been observed. From all of which it may be stated, that nasal accessory sinus disease, in the large majority of cases, results from nasal catarrh; that

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it begins insidiously ; and that, in the early stages, it improves or even actually recovers during the warmer months of the year, recurs during the autumn and winter, and ultimately becomes permanent.

Treatment should therefore begin with the conditions in the nose itself, which tend to perpetuate a nasal catarrh, to propagate it towards the accessory sinuses, and to hinder the natural recovery of the catarrhal sinusitis when this has resulted. At the same time, where it is possible, the patient should be advised to live in a climate or locality and under conditions which render the recurrence of nasal catarrh and catarrhal sinusitis less prone to take place. High and dry localities are preferable to low and damp, and inland to seaside. Avoidance of the cold and damp of the British Isles during the winter months is only possible to the few. Stuffy and over-heated atmospheres should be avoided. Graduated exercises are beneficial on account of their good effect upon the general health and on the nasal mucous membrane. Cold douching of the head and chest, and cold bathing are sometimes very helpful. Too much coddling in the way of clothing is harmful, but the one thing needful is thick and strong footwear. Food should not be of the heavy variety, and hot liquids should be avoided, as well as heavy wines. One's experience, indeed, is that all alcoholic beverages tend to cause congestion of the nasal mucosa. *Verb. sap.* Cigarette smoking is bad in this connection. One is sometimes asked as to motoring, and one's reply is that provided attention is paid to bodily warmth, it need not be proscribed.

While the foregoing remarks apply especially to cases of, what may be termed, recurrent catarrhal sinusitis, cases in which by preventing the recurrence of the catarrhal condition the changes in the lining membrane of the sinus involved may naturally recover, they are applicable, too, as adjuncts to the special line of treatment adopted for a sinusitis fully established. This means the majority of cases which come before the rhinologist. But before discussing these cases of chronic suppurative sinusitis, let me say a few words with reference to the treatment of acute sinusitis.

Acute catarrh going on to suppuration may affect any or all of the sinuses, and the first aim should be to permit the discharge, which is frequently under great tension, to

escape. The hindrance to this is usually the congestion and swelling of the mucous membrane around the opening of the sinus into the nose. This tends to subside of itself in two or three days, but to expedite this, warm, alkaline, nasal douches are helpful, and they may with advantage be followed by a spray of menthol, camphor, eucalyptus or some similar substance in parolein. The most valuable application, however, is adrenalin solution. It should not, however, be used too strong, for the reaction may give rise to increased congestion and intense pain. A dilution of 1 in 10,000 or 1 in 20,000 should be used. Many rhinologists combine cocaine with it, but the writer is of opinion that cocaine is much too freely prescribed in the treatment of nasal affections. The adrenalin solution may be used as a spray, or it may, where circumstances make it possible, be applied directly to the region of the opening of the particular sinus involved.

Internally, opium is of value in reducing the congestion of the mucous membrane, and of its various preparations one gives the preference to Tinct. Camph. Co. Other drugs which relieve the pain, which is often severe, are salicylate of soda, phenacetin, and such like. A purge should be given, the patient should be kept in a warm atmosphere, and the steam kettle, with or without Tinct. Benzoin. Co., may be employed. These simple methods suffice in the majority of cases of acute sinusitis to bring about recovery.

Occasionally, however, other steps are required. These will, to a certain extent, vary with the sinus affected. The first requisite is a very careful examination of the region of the communication of the sinus with the nasal cavity. This means the region of the middle meatus in sinusitis of the anterior group, that is, the larger proportion of cases. When the posterior group is involved, the region between the middle turbinate and the septum, or more exactly above the middle turbinate, or the superior meatus, claims attention. The careful application of pledgets of cotton-wool soaked in cocaine and adrenalin solution to these parts may so contract the mucous membrane as to overcome the occlusion of the ostium, rendering it possible, if the purulent contents of the cavity do not escape, to pass a canula into the sinus and wash it out. In acute cases, however, this procedure should be most carefully

carried out. Frequently, it is impossible.

In dealing with the maxillary antrum, lavage by the inferior meatal route is preferable. When it has not been possible to liberate the contents of the frontal or sphenoidal sinuses either with or without the aid of the canula, the next step is the removal of the anterior part of the middle turbinate in frontal sinusitis, or the whole in sphenoidal sinusitis. This, too, may be called for in acute ethmoidal disease, and occasionally in dealing with antral disease, one adopts a similar procedure as regards the anterior end, but, as a very general rule, lavage by way of the inferior meatus is all that is required.

In all cases of sinusitis, however, with a view to the prevention of recurrence, if the middle turbinate has not already been dealt with, it should be removed in part or wholly, where by its size it causes pressure on the external nasal wall and interferes with the patency of the openings of the sinuses into the nose. For the same reason, a septal deflection in this region should be remedied. When once a sinus has evacuated itself of its contents or been evacuated in acute sinusitis, the mucous membrane around its ostium contracts, so it is very rarely that lavage a second time is called for, or that an external or more radical operation is required. In those extremely rare cases, of which, however, a few have been recorded in which intracranial symptoms have shown themselves, in the course of acute frontal and sphenoidal sinusitis, one must act with a proper regard for the seriousness of the condition.

We now come to the much larger subject of chronic sinusitis, and in considering the treatment of this condition, it will be advisable to take the sinuses separately.

Ethmoidal Disease.—This is considered first, because ethmoidal disease is commonly associated with disease of the other sinuses, and it will save repetition if we consider it now. Moreover, the eradication of this condition may be sufficient to permit the catarrhal or suppurative process, which has extended into one or more of the larger sinuses, to recover of itself. The disease in the ethmoid may be localized to one cell, the ethmoidal bulla, for example, or the whole ethmoidal labyrinth may be affected. Some rhinologists speak of closed and open ethmoidal disease, according to whether the

discharge escapes freely from the cell or is pent up in it. This nicety of division, however, concerns diagnosis rather than treatment. Polypi are commonly associated with ethmoidal disease, and when large may have to be removed as a preliminary procedure. When the disease is extensive and when the posterior cells are involved, the middle turbinate must be removed. This can be dispensed with, when the suppurative process is localized to one or more of the anterior cells. The cells themselves may be oblated by means of punch-forceps, of which various patterns are in use, or—and this is the method the writer usually adopts—the cells can be thoroughly removed by means of the ring curette, according to the method advocated by Lack. Care must be taken to work from behind, downwards and forwards. Firm pressure on the curette is employed. Cocaine anæsthesia, except in the very nervous, is sufficient, and the whole of the ethmoidal cells, where necessary, can be removed at one operation. This method seems preferable to that of Mosher, who works backwards and downwards. Removal of the ethmoidal cells by an external incision is part of the complete frontal sinus operation, but apart from this it is sometimes carried out when orbital abscess has resulted from ethmoidal disease. Even when this complication is present, and indeed under all circumstances, the writer prefers the intranasal operation if it is at all feasible. Whatever method is adopted, the position of the cribriform plate should be borne in mind, and great care exercised in working in its neighbourhood.

Maxillary Sinusitis or Antral Disease.—As a preliminary to the treatment of this disease, not only should any contributory nasal condition be remedied, but the teeth of the upper jaw should receive attention. This applies especially to the second premolar and to the first and second molars, and not only are obviously decayed teeth suspect, but the cause may lie in a tooth which has been stopped and at whose root diseased processes may still be active. Too conservative dentistry has not infrequently resulted in antral disease.

Having attended to the nose and the teeth, we have then to consider whether the disease is likely to be amenable to treatment by repeated lavage, or whether an operation will be necessary, and if the latter, what extent of operative procedure

Unfortunately, we receive no definite guidance in this relation from the appearance of the discharge, from its bacteriological examination, from the result of the transillumination test, or from skiagraphy. One naturally looks upon a sinusitis with stinking purulent discharge as less likely to benefit from lavage than one with a flocculent muco-purulent discharge, and the less purulent the discharge the more hopeful one is that an operation may be avoided.

Again, though one does not base too much significance on the transillumination test by itself, one is less hopeful of a case when the cheek is quite black than of one in which it illuminates somewhat, and the crescent is present though dimmed. One is not surprised, however, if, in what appears to be a mild case, repeated lavage causes no benefit, while, on the other hand, one has occasionally seen a second lavage of an antral cavity, which on a previous occasion gave a positive result with stinking thick pus, prove absolutely negative, the fluid returning as clear as it was introduced. On the whole, however, one may say that a fair proportion of mild cases, that is of cases more catarrhal than purulent, recover under repeated lavage, while only rarely does this method effect a cure in cases manifestly purulent. Occasionally one lavage results in a cure, or an apparent cure. In such a case, one should wait for two or three weeks and wash out again before accepting the cure as definite, for recurrence is probable.

How often should one repeat the lavage before resorting to an operation? This will depend on a general survey of the case, or the opinion one has formed of the likelihood of the repeated lavage leading to a cessation of the discharge, as well as on the progress of the case as shown by the discharge removed in successive lavages. On the Continent, this procedure is persevered in for a much longer time than in this country. Probably with us neither the surgeon nor the patient would, in most instances, be willing to repeat it more than six or eight times, though the writer treated one case to a successful issue by 25 lavages at intervals of one week at first, increased later to several weeks. Once or twice the lavages resulted negatively, that is, the fluid returned clear, but on the next occasion a positive result was again obtained. In the end, however, the cure was definite and remains after

several years. Boracic lotion is probably as good as anything, though others make use of other mild antiseptics or even of sterile water.

As for lavage for diagnostic purposes, the author prefers the inferior meatal way with Lichwitz's cannula. The lotion can be introduced either by gravitation or by some form of syringe, and the lavage should be continued till the lotion returns clear, the patient during the procedure holding his head forwards and face somewhat downwards, breathing all the time through his mouth. The cavity is then dried by blowing through the cannula with an air bag, and I then introduce rectified spirit. Though in a fair number this method of treatment results in a cure in the majority of cases of antral disease operation is sooner or later called for. One has then to consider what particular form of operative procedure is advisable.

The old method of draining through the alveolus has rightly fallen into disuse, by rhinologists at any rate. It is unhygienic in character, and probably could only lead to a cure in cases which are better treated by lavage through the inferior meatal wall. I have no doubt it frequently made the condition of the lining membrane of the antral cavity worse by fresh infection from the mouth, and it certainly at times left an opening into the antrum which was obliterated only with some little difficulty. The method, however, it seems to me, provides a warning not to expect too much from the simple intra-nasal opening of the antrum. This brings me to the two types of antral operation, intra-nasal and external, or rather, by way of the canine fossa under the upper lip.

The intra-nasal operation consists in making an opening into the antrum by removing the anterior portion of the antro-nasal wall in the region of the inferior meatus, and of the anterior end of the inferior turbinate, if this be, as it usually is, necessary to obtain free drainage. The opening is enlarged by removing the bone in a forward direction and by levelling the base of the antro-nasal partition, special forceps being employed for these purposes. The antral cavity can then be inspected more or less completely by the aid of specially designed specula and mirrors. The after-

treatment by washing out through a bent cannula can be carried out by the patient himself. Certain rhinologists still favour this method, though probably it has not the vogue it had a few years ago. The writer, when he does employ it, always does so with a mental protest, in much the same frame of mind that he employs the modified radical mastoid operation. One cannot be sure that the more radical method may not be later required.

The addition of curettage of the antrum through the nose, which cannot be thoroughly carried out, or the making of a much larger breach in the antro-nasal wall, which some advocate, to prevent the closure of the opening by the sprouting of granulations which arise from the irritation of the discharge, adds to the severity of the operation and destroys the special advantage which is claimed for the simple intra-nasal opening. It will be shown, however, that the radical antral operation need not be of so severe a nature as to give a strong reason for this simpler method, and certainly one feels that unless the inequality in severity is great it is preferable to adopt a method by which the interior of the antrum can be thoroughly inspected. In dealing with the frontal sinus, on the other hand, a very strong case can be made out for a simple intra-nasal operation, even though in a proportion of cases it does not lead to a cure, for the complete external operation for frontal sinusitis is a more severe proceeding, and has a distinct fatality.

The radical antral operation, or the Caldwell-Luc operation, consists essentially in opening the antral cavity through the canine fossa under the upper lip, removing the diseased lining membrane, and making a counter opening into the nose in the region of the anterior part of the inferior meatus. The method of carrying this out will be better understood, if I describe my own procedure. In the large majority of cases, local anæsthesia is employed. A dose of omnopon, morphia, or some such sedative may be given previously. The antral cavity is washed out, and then dried by means of the air bag. I then inject through the cannula a small quantity of a mixture of 15 per cent. cocaine solution and adrenalin, following this by a gentle insufflation of air to spread it over the cavity; or the solution may be sprayed through the cannula. Cotton-

wool pledgets soaked in the same solution are then introduced into the anterior part of the nasal fossa. The region of the canine fossa is anæsthetized by the injection of a 2 per cent. solution of novocaine or alypin in normal saline, with the addition of a few drops of 1 in 1,000 adrenalin solution. In ten minutes, the mouth and teeth having been cleansed and the face painted with iodine, the operation can be commenced.

The anterior end of the inferior turbinate, if it is at all likely to interfere with the subsequent opening into the nose, and this means in most cases, is removed. It seems to me most unwise to risk the success of the operation by preserving the extremity of the inferior turbinate, for fear of dire results which, in my experience, do not arise. The nose is then lightly packed. The face is turned towards the side of the operation, and a plug of gauze is placed inside that cheek to catch any blood which may flow from the incision in the mucous membrane. This incision is made down to to the bone, and the writer makes use of an incision almost vertical, preferring it for several reasons to the transverse which is usually employed.

The periosteum is separated for a diameter of half-an-inch or more, and the antrum is opened by means of a chisel. A burr or small trephine is equally convenient for this purpose. The opening is enlarged forwards, so as to obliterate the angle, and down to the alveolus by punch-forceps. An inspection of the cavity can then be made. Occasionally, when the œdematous change in the lining membrane is localized, I content myself with removing the diseased part, but, as a rule, my practice is to remove the membrane completely by peeling it from the bony wall or by curetting it, special care being given to the malar angle, the alveolar region, and to the upper and anterior narrow recess between the nasal wall and the external antral wall. In these parts, the œdematous change is usually most marked. The success of the operation depends on attention to detail. If bony septal formations are found in the cavity, these are removed, no "dead" areas being left. Care is exercised in curetting the roof.

When one is satisfied that the cavity is clean, an opening is made from the antral side through the naso-antral wall in

the lower anterior part. The bone is removed by punch-forceps forward to the anterior angle, downwards to the floor (this is important), and upwards as far as the attachment of the inferior turbinate. In this way, the anterior third or so of the antro-nasal wall in the inferior meatal region is removed. The nasal mucous membrane is still unperforated. With a knife, a flap is made of this by dividing it superiorly, anteriorly, and posteriorly, and the flap so made is brought into the antrum. This covers the rough surface between the floor of the nose and the floor of the antrum, where the antro-nasal wall has been removed. The packing which has been in the nose is removed, and a light packing is passed into the antrum through the nose. The incision in the mucous membrane over the canine fossa is closed with catgut.

This is the procedure which I have adopted now in a large number of cases, and I have found it most satisfactory. Under the method of local anæsthesia described, it is almost bloodless, and 15 or 20 minutes gives ample time. Sometimes, for various reasons, one makes use of general anæsthesia or of combined general and local, and the comfort of the operation depends much on the anæsthetist. The packing is removed in 48 hours. In the after-treatment, the nasal cavity is gently douched once, or, if necessary, twice a day, and every three or four days, for a fortnight or so, a cannula is passed into the antrum through the nose and the cavity washed out. Usually there is a little swelling of the cheek for a few days, very rarely an actual cellulitis occurs, and still more rarely an abscess. Spreading osteomyelitis, either as a result of antral disease or following an operation on the antral cavity, is extremely rare, and the same holds for pyæmia.

The older method, in which no counter-opening is made into the nose, the after-treatment being conducted through the opening in the canine fossa, is not so satisfactory as that just described, and sometimes a permanent opening has been left.

In Denker's operation, the incision in the gingivo-labial mucous membrane is made nearer the middle line, over the junction of the antro-nasal and external antral walls. The antrum is opened, and the prominent anterior angle, and the adjacent portions of the antro-nasal and external walls are

removed. This certainly admits of a thorough inspection of the cavity, but disfigurement results from falling in of the soft parts at the junction of the ala nasi with the upper lip, a disadvantage which outweighs any advantage the method may have.

Other methods of operating on the antrum have been employed, but actually, in this country, the only two which are generally adopted are intra-nasal operation and the Caldwell-Luc.

Frontal Sinusitis.—In approaching the question of operation on the frontal sinus, certain considerations present themselves which make one adopt a different attitude to what one takes in dealing with antral disease. Disease of the frontal sinus is, fortunately, not nearly as common as disease of the maxillary antrum. Instead of the fronto-nasal opening being situated, like the antro-nasal, badly for drainage, it is particularly well placed for this purpose. Frontal sinusitis, is, however, the more serious condition from the position of the cavity in relation to the intracranial contents. Though intracranial complications are much less common than with aural suppuration, they do occur, and as regards brain abscess this may be present some time in the "silent" frontal lobe before giving rise to any marked signs of its presence. At the same time, one must not allow the possibility of intracranial complications as a result of the disease to loom too largely in one's mind in considering the treatment of frontal sinusitis.

Again, frontal sinusitis sometimes causes intense suffering in the shape of pain and depression, much more so than antral disease, though these and especially depression are by no means unknown with the latter. On the other hand, as has already been remarked, a radical and effective operative procedure on the frontal sinus is a formidable affair, and has a distinct mortality, chiefly from two possibilities, direct intracranial infection and spreading osteomyelitis of the frontal bone going on to infection of the meninges. The disfigurement, too, which may follow even a successful external operation, must be taken into account. At the same time, one has to bear in mind that, in most cases, the disease in the sinus is, as one would expect, in the most dependant part. This may mean just on the frontal side of the fronto-

nasal opening, though it may mean much more than this in a large sinus, when the floor extends more or less above the orbital cavity and deeply almost to the sphenoid. The extent of the sinus can, however, usually be determined by X-ray examination, which should never be omitted.

The relationships of the fronto-ethmoidal cell which varies much in size and position, and of the upper anterior ethmoidal cells introduce another factor, and one must as well take into consideration the proximity of the vulnerable cribriform plate to the fronto-nasal passage. It will thus be seen how necessary it is to adopt a judicious attitude towards the question of the treatment of frontal sinusitis, and how difficult it is to decide on the appropriate operative procedure in any given case. There is room both for the partial or intra-nasal operation and for the radical external, but it would be altogether unwise to tie oneself to either method for all cases. At the present moment, the intra-nasal method has strong advocates, but neither method is free from danger and only prolonged experience will lead to a proper appreciation of their merits.

As in antral disease so in chronic frontal sinusitis, there are mild cases in which lavage, several times repeated, followed by the introduction of rectified spirit, is all that is required. Lavage of the frontal sinus, however, is not always easy, and, to facilitate it, it may be necessary to remove the anterior end of the middle turbinate and the ethmoidal cells in the region of the ostium. Indeed, in all cases the outlet from the sinus must be freed from obstruction, whether due to the middle turbinate, a high septal deflection, or ethmoidal condition. When lavage fails to cure the disease or, at any rate, to keep the discharge in check, one may proceed to carry out what is known as the intra-nasal operation. Various methods and various instruments have been adopted for this purpose, which aims at enlarging the fronto-nasal opening and removing the disease from the lower part of the sinus. Indeed, an attempt has been made to carry the curettage still further into the sinus, though this cannot be recommended. The one thing needful is a thorough knowledge of the anatomy of the parts and of the pitfalls to be avoided. Without this the risks are even greater than with the external operation.

Sometimes the procedure is very simple; at other times,

owing to anatomical variations, it is much more difficult. It can be carried out under local or general anæsthesia, and subsequently the cavity can easily be washed out. As with the intra-nasal operation on the antrum, one must always foresee the possibility of having later to proceed to a more radical external operation.

The external operation on the frontal sinus, as at present performed, is the outcome of the results obtained by older and more limited methods. The opening of the anterior wall, even with curettage of the lining membrane as fully as this can be carried out, is practically without avail as far as curing the disease is concerned, nor is the result much better even when the whole of the wall is removed. When the disease is extensive, the only procedure which holds out hope of a successful result is complete removal of the anterior wall and floor, and with these the whole of the diseased lining membrane, together with enlargement as far as possible of the passage into the nose.

Killian's operation has been devised to effect this. A curved incision is made over the prominence of the eyebrow from about the middle towards the nose, and then down the side of the nose to the level of the inner canthus. This incision goes down to the periosteum and the soft parts are reflected. Two parallel incisions a short distance apart are made through the periosteum over the most prominent part of the bone, for it is intended to retain a narrow bridge of bone. This slightly risks the success of the operation, but it preserves the contour of the brow and lessens disfigurement. The anterior wall is then opened and removed, and the floor likewise, both in their whole extent, all diseased tissue being at the same time eradicated. Care is taken to keep intact the narrow bridge between the anterior wall and floor. The fronto-nasal passage is enlarged as much as possible, the ethmoidal cells being removed for this purpose.

When, as is usual, there is ethmoidal disease as well, Killian's complete operation is performed. The skin incision is continued slightly downwards, the upper part of the ascending process of the maxilla is temporarily resected, and the ethmoidal cells removed. If there is sphenoidal disease as well, that sinus can readily be opened into through this incision and curetted.

The middle turbinate is removed, if this has not already been done, and a rubber tube is passed down into the nose. The incision may be closed at once or after a day or two. Firm bandaging crowds the soft parts into the cavity of the bone both anteriorly and from below, the aim of the operation being to obliterate the sinus. The writer removes the tube in a couple of days, keeps the nasal passage clear by douching, and removes granulations from the region of the antro-nasal passage if they become exuberant. A spray of 1 in 500 formalin solution is useful for this purpose, as well as in the after-treatment of ethmoidal and sphenoidal disease.

As a very general rule, the post-operative course is without incident, except for some swelling of the eyelids, or a temporary diplopia from interference with the attachment of the superior oblique. One must, however, be on the look-out for signs of intracranial complications or of osteomyelitis, in the treatment of which early and thorough measures give the only hope of avoiding a fatal issue. It can readily be understood that, with a view to obviating various drawbacks in connection with an operation on the frontal sinus, various methods and modifications of methods, differing in detail from what has been outlined, have been advocated. In this country, Watson Williams has devised a modification which has given him good results. One's aim is to remove the disease, to prevent its recurrence, and at the same time to cause as little disfigurement as possible.

When both frontal sinuses are affected, one may attack them through separate incisions, which has seemed to the writer the better way, or a vertical incision over the middle of the forehead above the root of the nose may be employed.

Sphenoidal Sinus.—Chronic sphenoidal sinusitis, of a mild degree, at any rate, is probably much more common than is generally supposed, and though the effect on the general health is nothing like so baneful as that caused by antral and frontal sinus disease, it often gives rise to much discomfort by the continued post-nasal discharge. Nasal sprays and douches give temporary relief, and one hesitates often to advise more active treatment. It is not always easy to wash out the sphenoidal cavity without first removing the middle turbinate, but this may be performed as a preliminary to operation on the sinus

itself. When there is posterior ethmoidal disease, a not uncommon association, these cells should be opened and removed. It is then easy to open into the sphenoidal sinus through the ordinary ostium.

My own plan is to pass a spoon through this region with the convexity towards the roof and outer wall, and then to break down the anterior wall. The use of perforators to open the sinus has always seemed to me objectionable, because of the risk of injury by perforating the roof where this bulges markedly, as it does in a fair proportion of cases, into the cavity. In whatever way the sinus is entered, it is very necessary to remove the anterior wall completely. The lining is curetted, care being observed along the external wall and especially along the roof. The changes in the lining membrane are found chiefly in the floor and in the antero-lateral recess. Septal formations in the cavity must be destroyed. The variations in the size and in the relations of the sinus to its fellow of the opposite side and to the posterior ethmoidal cell must be borne in mind. It should be recognized as well that delay in the cure of a sphenoidal sinusitis after operation may be due to abnormal anatomical conditions.

Pansinusitis.—When all the accessory nasal sinuses are diseased, one has to deal with a condition of pansinusitis. In such a case, unless there are indications which make another course advisable, it is well to deal first with the antral, ethmoidal, and sphenoidal conditions, and later with the frontal, if that should then be necessary.

A word or two may be added with reference to the employment of vaccines in the treatment of sinusitis. These may be used to treat mild or recurrent cases, in the same way that they are employed, and with advantage, in recurrent nasal catarrh ; that is, a course is given previous to the period, the autumn or winter, at which nasal catarrh recurs. Vaccines may be used too, and one has so used them, as an adjunct to operation. Used alone as a method of treatment of fully established sinusitis, their value is not great.

THE PREVENTIVE TREATMENT OF CATARRHAL DEAFNESS.

By MACLEOD YEARSLEY, F.R.C.S.

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MIDDLE ear deafness of catarrhal origin is one of those conditions which, once it has gained a firm hold, baffles the otologist. Treatment of its later stages is disappointing, and the only methods that are of any real avail are those of inflation, the bougie, and otomassage; even these fail after a time. Otological literature is full of new therapeutic measures, most of which have but a meteoric existence or recur at intervals, like comets. Such methods as the permeatal application of superheated air, intratympanic injections of dog's gastric juice, and injections of thiosinamin or its derivative fibrolysin, are examples of these short-lived remedies.

Recently, "re-education of the hearing" has competed with radium as a sort of universal panacea, but the short paper contributed by Muecke (*B.M.J.*, December 12, 1914), has shown that its results are no better than those achieved by the Eustachian catheter, the bougie, and simple otomassage. Indeed, I have more than once satisfied myself that certain greatly extolled remedies have owed their success not to themselves but to the regular inflation, with or without otomassage and the use of the bougie, that accompanied them.

Chronic middle ear catarrh does not appear to be honoured with the same attention at the hands of the otological societies that middle ear suppuration has received; probably because the latter condition provides the greater satisfaction of brilliant and successful operations. Analysis of the Proceedings of the Otological Section of the Royal Society of Medicine for the Session 1913–14 shows that, of 43 items before its meetings, 14 dealt with suppuration and its complications, but only one with catarrhal conditions; and that was the exhibition of a

new Eustachian bougie.

The question naturally arises: Why is it that, whilst the achievements of modern otology have been so brilliant in saving life (and, occasionally, hearing) in chronic suppuration, so little has been done for the amelioration of the permanent and distressing disabilities resulting from progressive catarrhal deafness? The answer is contained in one statement: Because otology has not yet grasped the full significance and importance of *prevention*. It has been said recently by a well-known American aural surgeon that the mission of the physician is threefold: To prevent, to cure, and to alleviate; and that in otology this mission seems to have been reversed, and reads: To alleviate, to cure, and to prevent. Since in the great majority of cases chronic catarrhal deafness originates in conditions of the nose and nasopharynx, and that this fact is well known, there is no reason why a high percentage of such cases should not be prevented. It is clearly the duty of the specialist to educate the general practitioner in this important matter, and for the two to combine to teach the public the grave necessity for not neglecting such cases at their inception. The time to treat chronic middle ear catarrh is before it has arrived; it is the first onset of deafness or tinnitus that calls for prompt and serious interference. There is too much half-heartedness, in some instances almost amounting to timidity, in dealing with these cases. It is as useless to play with them by nasal douches and applications of the galvanocautery to the turbinates as it is to treat effects without dealing with causes. Patients are frequently to blame for not applying earlier for treatment, but they at least have the excuse of ignorance in many cases, and this ignorance is too often fostered by the pessimistic verdict that "nothing can be done for middle ear catarrh" offered as a solace by so many practitioners, and echoed, parrot-like, by ignorant laymen.

A large number of cases of chronic catarrhal deafness owe their origin to neglected or imperfectly treated adenoids in childhood. Often too little attention is paid to adenoid extensions in Rosenmüller's fossæ or to after-treatment of the nasal cavities. It is a common thing to find that adults suffering from chronic middle ear catarrh, volunteer the statement that

they suffered during childhood from recurrent attacks of earache. Many of these cases, when examined by the posterior rhinoscope, or by some form of nasopharyngoscope, show that the Eustachian openings are hampered in their normal ventilating function by adhesions in Rosenmüller's fossæ, left by adenoids that have retrogressed or have been operated upon imperfectly. These cases need not be alluded to further, for their prevention is obvious. It is common to find the history given by parents that an operation has been done for adenoids at a large general hospital, but that the child has since been more deaf. The rational treatment of adenoids, especially as regards *efficient* operation and careful after-treatment, has yet to be more fully appreciated and carried out. Acute tubotympanic catarrh is the beginning of most middle ear disease, and better care of the throats of children suffering from the ordinary infectious diseases is needed.

The varieties of middle ear catarrh which must especially be distinguished are two: those in which the condition is due to repeated attacks of acute nasal and nasopharyngeal catarrh—to ordinary colds; and those in which a gradual and insidious progressive deafness occurs without any special history of frequent colds. In both of these, however, the primary cause is practically the same—a badly drained nose. Almost every variety of nasal abnormality may be found in the cases in both categories; but the great majority shows deformities of the septum, usually accompanied by enlarged posterior ends of the inferior turbinates. The septal deformities noted range from marked deflections to small spurs. Many large spurs are but low-situated acute deflections with thickened convexities. The effects of serious and obstructive deflections are too well known to require detailed description. It is not necessary, however, for a marked deflection to be present for serious middle ear trouble to result. Indeed, it is the comparatively slight deflection which is manifested by a crest situated low down, near the floor of the nose, that often has the worst effect upon nasal drainage. This is accentuated by the fact that, too often, the effect is not fully appreciated and temporizing methods by douches and the like are employed when the spur ought to be removed. Such inferior deflections and spurs tend to direct nasal secretions into the nasopharynx,

where their more or less continuous and irritating presence causes a chronic nasopharyngitis which, sooner or later, spreads to the Eustachian tubes and middle ear. This imperfect nasal drainage tends also to such disarrangement of vaso-motor function that makes microbic infection easy, and frequent attacks of "cold" result. This is further predisposed to by the fact that the conformation of the abnormality is often such as to create nooks and corners in which micro-organisms can find comfortable bases from which to act.

The aural history of these cases is usually one of attacks of deafness during colds. The earlier ones are recovered from completely, but a time arrives when each attack leaves the patient more deaf; then a stage is reached when deafness is permanent, and each cold leaves it accentuated. The right time for treatment is before this stage is reached; all measures taken later can only be palliative.

Another form of nasal abnormality, which is a prolific source of catarrhal middle-ear deafness, is the bony spur situated far back in the nasal cavity. The septum itself is often quite straight or but very little deflected in front. This spur appears by anterior rhinoscopy as a pointed or conical projection, opposite the posterior part of the inferior turbinate; frequently it comes into view only during the ischæmic effect of an application of cocaine and adrenalin. In reality, the outgrowth is more of the nature of a semicircular ledge of bone growing from the lower part of the bony septum, like a semicircular doorstep, and having a strip of cartilage around its convex, vertical face. From close observation of many cases, I am of opinion that this form of septal spur—which is very common—is one of the most potent of nasal abnormalities in the causation of chronic middle-ear catarrh. It acts as a constant source of irritation to the inferior turbinate at its hinder end, causing it to become enlarged. The determining cause of this irritation may be either that the spur, growing gradually, at last reaches such dimensions as to come into contact with the turbinate; or the turgescence of the turbinate during a cold is sufficient at some period to bring it into contact with the spur. This contact is enough to establish an irritation which prevents the turgescence from subsiding, and a permanently enlarged posterior end is the

result.

When the posterior end of the inferior turbinate is enlarged, the glands in its mucous membrane partake in the hypertrophy. Secretions from these glands are consequently increased, and, entering the nasopharynx, irritate it, and cause a catarrhal condition, which quickly becomes chronic. These secretions are nearly always more abundant at night, because the posterior end becomes more turgescent from the effect of gravity in the recumbent posture, and they then flow directly over the Eustachian cushion. Examination by means of the naso-pharyngoscope will often show the cushions of the Eustachian tubes swollen and congested, and, when the condition has been operative for any length of time, granular.

Probably, too, the form of bony spur just described may sometimes act by directing the incoming current of air on to the lateral wall of the nasopharynx and on to the Eustachian opening. When such a spur is present, the result upon the ear may be the catarrhal form of median otitis, starting with a cold and progressing with exacerbations, or the slow, insidious form of catarrh without any special reference to colds. I am of opinion that the latter variety of chronic catarrh is nearly always due to the effects of these spurs.

One word on the question of the ear earliest affected. Chronic catarrhal deafness usually begins in one ear; sometimes it is not until the other is attacked that the deafness is realized. In an analysis of cases, I find that the side first affected often shows some relation to the side on which the the nasal deformity exists. So far as I can gather, the side first affected is that upon which the patient is in the habit of lying during sleep. It can readily be understood that irritating secretions in the nasopharynx would gravitate to the side which is the lower, so that the lower Eustachian tube is the one more frequently—possibly the only one—exposed to their action.

Now the conditions just described, as those most often found to be conducive to middle-ear catarrh, are well-known to every rhinologist and otologist, yet their importance from the point of view of treatment does not seem to have commanded the attention that it merits.

The general line of treatment which seems to be adopted when a patient presents himself with early middle ear catarrh

is to have recourse at once to inflation by catheter or Politzer bag, and, so far as the nose is concerned, to be content with prescribing a nasal douche, a spray, or a snuff, with, perhaps, the addition of an occasional application of the galvano-cautery to the turbinates. If the case is in an early stage, or has not yet progressed very far, the result is good. It is, however, good only for a time ; relapse comes presently and more inflation, more nasal douching, more cautery are tried, probably with less success. Relapse occurs in nine cases out of ten, for the cause has not been treated adequately. Often then only is serious correction of nasal abnormality attempted : when it is too late. Perhaps more enterprise is shown by direct local treatment of the nasopharynx, but, unless the cause of the nasopharyngeal condition is carefully sought out and treated, ultimate failure is inevitable.

The proper course to pursue in dealing with these cases is : first, to make a complete physical and functional examination of the ear, so that its exact condition as regards tympanum, Eustachian tube, and hearing, is recognized ; secondly, to examine the nasopharynx and nasal cavities to ascertain their condition and causative relation to the affected ear or ears ; and thirdly, to adapt treatment judiciously to the individual case, always bearing in mind that the removal of the cause is of paramount importance. A few words upon each of these three heads is necessary.

In examining the ear, the condition of the membrana tympani and of the Eustachian tube must be ascertained, but the results of functional testing by whispered and spoken speech and by tuning forks is of equal if not of greater importance. Speech is the most useful test, not only from the point of view of prognosis, but for ascertaining the progress of the case during treatment. My own experience goes to show that, so long as any whisper-hearing remains, the prognosis is encouraging, being better in direct proportion to the amount retained. As regards tuning-fork tests, if Rinne's reaction is negative only for low forks, especially if the disproportion between bone and air conduction is not very marked, prognosis is not bad. Another point in prognosis is the amount of loss of hearing by air for low tones. The smaller the reduction in low-tone hearing, the better the prognosis. When the loss is

up to and including the C 128 fork, Rinne is markedly negative or negative for both high and low forks (C 128 and C 512 are the best to use), and the whisper can no longer be distinguished, prognosis is bad. I ignore, here, the presence or absence of paracusis Willisii, for I am speaking rather of the early stages of catarrhal middle ear deafness. Moreover, the presence of this symptom means that both ears are seriously involved.

The second point concerns the examination of the nose and nasopharynx. The former should be inspected by anterior rhinoscopy, both without and with the use of cocaine and adrenalin. In no case should the routine examination of the nasal cavities under cocaine be omitted. It is sufficient gently to pass a wool-armed probe, dipped in a solution of equal parts of 10 per cent. cocaine and 1 in 100 epinin (or 1 in 1,000 adrenalin), over the mucous membrane of the anterior half of each nasal chamber. This is more efficient and less haphazard than the use of the spray. By this means sufficient ischæmia, without inconvenience to the patient, is obtained to ensure a full inspection of any abnormality of the septum present, and by it alone can the existence of a posterior bony spur be detected in many cases.

The nasopharynx can be examined by means of the posterior rhinoscopic mirror or by an electric nasopharyngoscope. It is better to use the former instrument before the nose is placed under cocaine, for the condition of the posterior ends of the inferior turbinates and of the Eustachian cushions can better be ascertained. For the electric nasopharyngoscope, it is usually necessary to cocainize the lower part of the septum. The instrument I prefer to employ is that of Holmes, which is passed like a Eustachian catheter and can be used from one side. This reveals well the condition of the post-nasal space, and by its means adhesions or growths in the ostium of the tube can be accurately observed.

Having ascertained with as much detail as possible the exact condition of the patient, including his general state of health, and especially that of his digestive and circulatory organs, then and then only can the question of treatment be considered. When the case is in an early stage and the prognosis is favourable, there can be no other course open

than to remove the cause. There can and must be no half measures. When a well-marked spur or deflection is present, the use of nasal douching, sprays, snuffs or the application of the cautery to the turbinates is merely playing with the case, and will lead eventually to disaster.

Here I would wish to say something as regards the use, or rather abuse, of the galvano-cautery, in dealing with the nose. Except in very rare cases, I have entirely abandoned this method for some time past, basing my conduct on the argument that when the septum is abnormal, a structural alteration is necessary, and that the less organs which have a distinct and active physiological function to perform are interfered with the better. I am pleased to find that the *Annals of Otology* for September, 1914 (Vol. XXIII., p. 563) contains a short paper by Wales entitled "Cauterisation of Mucous Membranes, Particularly of the Nasal Mucosa—A Protest." Calling attention to the fact that the function of the nose is the matter of greatest importance in the treatment of all nasal diseases, the author protests vigorously against the "reprehensible destruction of the nasal mucosa" by cauterization, which, he says, of any kind, almost without exception, should never be used in the nose. The exceptions are "those cases of hæmophylia or such conditions where it is necessary to save life." The nasal mucosa should be treated with the utmost gentleness. The strongest argument against cauterization of any kind is that a slight pathological condition is increased to a graver one. Wales sums up in a paragraph which should be printed in every text-book of rhinology: "Cauterization is a method of getting results without thought of final consequences. It is irrational and lessens the efficiency of the nose by destroying the integrity of the ciliated columnar epithelium, leaving in its place tissue which cannot carry on a single function of the nose." With these remarks, I am in complete agreement.

When a nose is ill-drained by reason of septal deformity, it is the septum that must be dealt with and not the turbinates. A few years ago, the operations dealing with the septum were mostly very unsatisfactory, and rhinologists often had to attack the turbinates in order to restore the patency of the nasal passages. Even then, however, a

cutting operation was better than the cautery. But with the modern submucous resection of the nasal septum ideal results can be obtained by the exercise of reasonable skill. This is the most scientific operation ever introduced into rhinology, since it gives good and permanent results, and can be adapted to any kind of deformity. Small spurs can be removed by other methods, but I am of opinion that, in the majority of cases, the resection operation for spurs, and especially for the posterior spur, is the most sure.

In very early cases, the effect of the restoration of the nose as to its proper function follows quickly, and, in some instances, the ears recover without further treatment. Others may require a short course of inflation, etc. The possible necessity of constitutional treatment in addition, must not be lost sight of.

When a case has already progressed considerably on the way to permanent deafness in one or both ears, there are two points that must be borne in mind in the decision as to treatment: the possibility of improvement or, failing that, the possibility of arresting the progress of the deafness. It is best, in these cases of doubt, to take the patient into one's confidence; to explain the exact nature of the condition and the possibilities of treatment on the one hand, and of leaving things alone on the other. It seems reasonable to expect that, in a certain number of cases, removal of the cause will at least arrest the progress of the effect. Indeed, I am morally certain that quite a third of these cases will retain what hearing is left to them, either permanently or for a longer period than would otherwise have obtained, if the determining cause in the nose and nasopharynx is corrected.

I do not pretend to assert that the conditions I have described are responsible for the origin of all cases of middle ear catarrh, but they are undoubtedly so in the great majority of them. A certain number of cases arise from the continued influence of toxæmias, of which I believe pyorrhœa and intestinal stasis to be the most frequent. In many instances, too, in which nasal conditions are directly responsible as causative factors, the catarrh is aggravated by such toxæmias, which are sometimes instrumental in keeping up the nasopharyngitis after the nose has been corrected.

RECENT WORK IN GYNÆCOLOGY.

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THE outbreak of the War in August profoundly affected the output of medical literature during the latter half of the year, and gynæcological literature has suffered with other branches of medical science.

UTERINE HÆMORRHAGE.

Considerable attention has been paid to the subject of uterine hæmorrhage both from an anatomical and therapeutical standpoint.

The "Pathologic Physiology of Uterine Bleeding" is considered by E. Novak in a paper published in the *Journal of the American Medical Association* for 1914, of which the following are the most important points in the author's summary.

1. Menstruation—a physiological phenomenon—should be the fundamental starting point in a study of pathological uterine bleeding.

2. The factors concerned in normal menstruation are:

a. An ultimate cause situated in the ductless gland chain, the ovary being the most important in this relation.

b. A nervous mechanism, essentially vasomotor in character.

c. The pelvic organs, particularly the uterus and its lining membrane.

3. The causes of abnormal uterine bleeding may therefore be grouped as:

a. Fundamental, involving disturbances of the internal secretions.

b. Nervous, exerting their effect mainly through vaso-

motor nerves.

c. Anatomical, in which structural changes are present in the uterus and other pelvic organs.

4. There is good reason to believe that much light will be thrown on the fundamental causes of uterine bleeding by clinical methods of study on the relation known to exist between the ductless glands and the sympathetic and cranio-sacral nervous system.

The recent studies in the function of the ductless glands seem to point the way to a better understanding, not only of the cause, but what is still more important, of the treatment of menstrual disorders, which are prone to test the therapeutic ingenuity of the practitioner to the uttermost. There are many individuals encountered in the practice of all of us, who whilst not being marked examples of the effects produced by absence of one or more internal secretions, yet are what may be termed "borderland cases," and in these menstrual irregularities are prone to occur in addition to other well-known signs. The marked effect produced by thyroid extract, in suitable doses, not only in amenorrhœa but in menorrhagia, is now well established. Although the same good effect cannot at present be claimed for pituitary or ovarian extracts, no doubt further research will enable us to obtain more reliable preparations and more guidance concerning their administration.

There is probably no branch of treatment in which the results have been so unsatisfactory in the past. Yet such disorders are exceedingly common, and for this reason alone demand careful study. To cite, for example, amenorrhœa, a symptom of everyday occurrence in practice, is usually treated by iron on the assumption that it is due to anæmia. But many such patients are not anæmic, and are not cured by iron, which should teach us to search for a further cause. The administration of thyroid produces marked benefit in such cases, and even if there be some anæmia, the combination of iron and thyroid is productive of a pronounced effect on menstruation. The same is true in the treatment of certain examples of menorrhagia—those in which no anatomico-pathological cause can be detected. But such treatment must be founded on accurate diagnosis, for nothing can be

more reprehensible than to employ these methods in the presence of a gross pathological lesion in the uterus or adnexæ.

Uterine bleeding is further treated by radium, which is the subject of a paper by Howard Kelly and C. F. Burnam, entitled "Radium in the Treatment of Uterine Hæmorrhage and Fibroid Tumours," published in the *Journal of the American Medical Association* for 1914, lxiii, p. 622.

Kelly and Burnam divide pathological uterine bleeding into four groups:—

1. Bleeding uteri without demonstrable lesions—the so-called myopathica hæmorrhagica.
2. Bleeding uteri in young girls—the cause of which may fall into those in group one or three.
3. Bleeding uteri from polypoid endometrium, *i.e.*, polypoid endometritis.
4. Bleeding myomatous uteri.

The technique advised is filtration through glass 0·5 mm. of platinum, 0·5 mm. of zinc foil, and 0·3 mm. of rubber. Such an apparatus suitably shaped is introduced into the uterine cavity. Cervical applications alone are found to be less reliable, demanding much more radiation to secure results. As a preliminary to the introduction of the radium, the patient is given nitrous oxide, and then thoroughly curetted and examined fully under complete anæsthesia.

The amounts used intra-uterine in the fibroid cases have varied from 30 m.g. to 560 m.g. and the time of application from one and a half hours to forty-eight.

In the young girl class, the amount of radium introduced has been as small as 12 m.g.

From their experience the authors draw the following conclusions:—

1. In the classes of cases cited, radium completely and permanently controls uterine hæmorrhage.
2. The rays have a specific and direct action upon fibroid tumours, causing them to disappear completely or be greatly reduced in size. Furthermore, it does not destroy the ovaries.
3. Radium can bring about a complete amenorrhœa at

any age.

4. The menopausal symptoms which follow the amenorrhœa are absent in 50 per cent. of cases, and mild in nearly all of them.
5. Intra-uterine radiation, in contradistinction to cervical or vaginal, is the method of choice. Abdominal radiation in conjunction may add to the rapidity of the results.
6. Radium radiation is preferable to surgical procedures in the large majority of cases. If radium fails, surgery may have a chance, and there can be no harm in the waiting.
7. Radium is preferable to the Röntgen rays, because it is simpler of application, acts more rapidly, and with more intensity on the uterus than upon the ovaries.

There is a distinct danger of infection resulting in metritis and salpingitis following this treatment, and it is to be noted that in one of the author's cases a pelvic abscess formed. The number of "fibroids" treated was 21, menorrhagia or metrorrhagia being present in 19.

The number of patients observed, and the time during which these observations have been carried out, are not sufficient to justify any change in the method of treating "fibroids." More information is required concerning after-results, especially the onset of degenerative changes. In one case, the treatment failed and surgical treatment was employed. There is probably no major operation performed at the present time, which yields more satisfactory results in the hands of a competent operator, than the removal of a fibroid. Fashion has decreed from time to time that a trial should be given to palliative methods, but each in turn has been found wanting and finally abandoned.

Now, radium enters the field, but it will require brilliant results and long-standing observations to establish supremacy over surgical treatment, which rids the patient for ever of a tumour that may at any time cause complications and sequelæ of a dangerous character.

The non-destructive effect on the ovaries is important, if it is proved, but the authors do not supply the proof.

RADIUM IN THE TREATMENT OF CANCER OF THE FEMALE GENITALIA.

A large number of papers have been published on the treatment of uterine and vaginal cancers by radium. In many, the authors seem to have lost that judicial sense of proportion, which is so frequently absent in the writing of the enthusiast for "new treatment." To extract the sweet drops of truth from such a mass of speculation and experiment daily becomes more difficult.

"Can radium cure cancer?" is the question that the patient reader wishes to ask. In seeking an answer, one is confronted with a collection of incomplete reports, wherein, perhaps, the after-history has not extended beyond a month or two, or is conspicuously absent. How then can the practitioner obtain the information necessary to guide his patients who are anxious to submit themselves to treatment by radium, when the statements of "authorities" at home and abroad are so much at variance? Let me attempt to answer this question, and to consider the place radium should occupy in our fight against this dread disease.

Radium is not a specific cure for cancer, and there is no justification for recommending radium in the place of operative treatment. It is further unjustifiable to submit an early carcinoma to prolonged radium treatment, for the chances of a successful operation are decreased by the delay. What, then, can be claimed for radium.

Cancers of the vagina or vulva, which can be irradiated directly, are favourably influenced, as shown in skin carcinomata.

Inoperable cases may be improved, pain, bleeding, and discharge undergoing diminution. Treatment by radium has in a few cases rendered subsequent operation possible by causing increased mobility of the uterus and some recurrences have for a time been favourably influenced. Here, however, a word of caution is necessary, for if the primary operation has been as extensive as should be done for uterine cancer, and if the disease recurs, radium treatment may cause sloughing and serious injury to the pelvic contents.

Thus, as far as its application to cancer in the female genitals is concerned, radium has not proved the wonderful remedy that enthusiasts would have us believe. Indeed, it

runs a risk, in consequence of the usual reaction, of being gradually discredited in favour of other methods.

ABDOMINAL CÆSAREAN SECTION FOR ECLAMPSIA.

Professor Reuben Peterson[1] has done good work in publishing a "Critical Review of 500 Published and Unpublished Cases of Abdominal Cæsarean Section for Eclampsia." The treatment of this serious complication of pregnancy is still the subject of much controversy throughout the medical world. In this country, palliative methods of treatment are most favoured, a fact which is emphasized by the small number of operations included in Peterson's list which have been performed in Great Britain.

The first successful Cæsarean section for eclampsia in Great Britain was done by the writer of this article, and a full account was published in the *Lancet*[2] for 1910. The reluctance to have recourse to operative treatment has been due to the study of mortality statistics compiled over a long series of years; these include many cases operated on at a time when the technique of Cæsarean section was not as perfect as it is to-day.

Moreover, if the operation is only employed, when other methods have been tried and have failed, or after repeated attempts to deliver have been made and the genital passage infected, then the mortality rate must still remain high. Peterson shows that under favourable circumstances the mortality of the operation is gradually diminishing, and in one series of sixty cases it was as low as 15 per cent. Further, the sooner the operation is done after the onset of the fits, the better is the result both to mother and child. If, moreover, the cause of the disease be some toxin or toxins elaborated by the fœtus or placenta, then the sooner both are removed the better for the patient.

To sum up, the best course to pursue would appear to be that after the first fit a consultation should be held to discuss the question of rapid delivery, and that method should be adopted which causes the least amount of disturbance to

[1] *American Journal of Obstetrics*, June, 1914.

[2] McCann: "Cæsarean Section in the Treatment of Eclampsia Gravidarum," *Lancet*, 1910, II., 789-792.

mother and child. Of all the methods, abdominal Cæsarean section is the one which causes the least disturbance, and for this reason is destined to take a more prominent place in the future treatment of this, the most dreaded complication of pregnancy.

THE EMPLOYMENT OF HYPOPHYSARY OPOTHERAPY IN GYNÆCOLOGICAL PRACTICE. ITS IMMEDIATE RESULTS.

In a series of over 400 cases, Jayle attempted to determine the immediate effect of the administration of a pituitary preparation upon patients affected with various utero-ovarian troubles. The gland selected was that of the ox prepared after the method of Chody. The preparation was administered subcutaneously. Each ampulla corresponds to 0·05 gm. of the posterior lobe. The injections were given every other day, beginning with one-fourth of an ampulla, the dosage being increased daily so that a whole ampulla was given as the fourth dose.

General reaction was noted at once; it consisted of blanching, colicky pains, headache, and insomnia.

Ten cases taken from the series are briefly reported, the following results being obtained: diminution and often complete arrest of uterine discharges, relief of pain arising from salpingitis, metritis, and parametritis; regulation of the menses; and control of hæmorrhage due to subinvolution metritis and sclerosis of the uterine vessels.

If these results are confirmed, then pituitary preparations will take an important place in our therapeutic armamentarium. But, as already stated, the preparations of pituitary gland obtainable in this country do not, at least in the writer's experience, fulfil the results expected of them.

THE QUESTION OF AUTO-INFECTION IN GYNÆCOLOGY.

Unfortunate results after gynæcological operations, even classed under the title "minor gynæcological operations," always bring up anew the question of autogenous or endogenous infection. For this reason Benthin examined 500 cases bacteriologically. The mortality in those with hæmolytic streptococci was 29·4 per cent., whilst in the cases in which they were not present it was 4·2 per cent. An attempt must be

made before the operation, to free the vaginal secretion from bacteria, especially from hæmolytic streptococci. The most effective method seems to be warm douches with 1 in 1,000 bichloride of mercury.

A warning is needed, owing to the "aseptic craze" exerting a dominating influence.

Disastrous consequences, due to defective preparation and disinfection, have resulted from the performance of trivial operations on the uterus and vagina, because the bacillus coli and not a streptococcus may be the active organism. But although the former may not lead to the death of the patient, yet the local effects may be such as to cause long continued or permanent suffering with important pathological changes in the uterus and adnexæ.

The discharge from a uterine cancer not infrequently contains streptococci, and their existence increases considerably the risk of any operation.

Too much stress, therefore, cannot be laid on thorough disinfection of the vulva, vagina, and cervical canal before any operation, however "trivial" it may be supposed to be. Vaginal injections should be comfortably warm, *not hot*, for the latter produce œdema of the vaginal walls and desquamation of epithelium, thus tending to retard the healing of any cut surface.

THE SIGNIFICANCE OF PAIN IN THE RIGHT ILIAC FOSSA IN YOUNG WOMEN.

This common symptom is the subject of a paper by Winslow.[1] Right-sided pain is usually thought to be due to appendicitis. The acute cases or the chronic cases with definite localizing symptoms are readily recognized. In this author's experience, this symptom in young women is often due to some other cause. Some are of undoubted hysterical or neurotic origin, but with some underlying physical cause.

He differentiates from enteroptosis by injecting the colon with bismuth and by X-rays; from nephroptosis, by palpation of the kidney under anæsthesia if necessary; from disease of the right tube, by vaginal examination. In several operations for supposed appendicitis, a small ovarian tumour was

[1] *Hosp. Bull. Univ. Med.*, 1914, X., 81.

found.

Cholelithiasis with distended gall-bladder may simulate appendicitis, but percussion over the gall-bladder will elicit marked tenderness, and the gall-bladder can be detected under anæsthesia if necessary. Stone in the right ureter gives urinary symptoms with blood in the urine. Abdominal crisis due to Meckel's diverticulum, perforating ulcers, intestinal obstruction, and pneumonia, particularly in children, are to be considered. In typhoid fever, the fever precedes the pain.

This author states, in conclusion, that he has come to believe that in young women, unless the symptoms of appendicitis are frank and clear, the condition is probably something else. Pain and tenderness in the right side without rigidity, elevation of temperature, and leucocytosis is usually not appendicitis. Again, apparently severe and long continued pain in the right side in girls is more likely to be neurotic than appendiceal. Pain may also be reflected from the pelvic organs or some of the other viscera, and the primary seat of the disturbance may be determined by a more careful examination.

There is probably no more common symptom in women than pain in one or other iliac region, and a careful examination is needed to determine the cause. Most frequently the pain is intestinal in origin, originating in the cæcum and appendix on the right side and the sigmoid colon on the left. The ovaries, however, are too frequently blamed, and the treatment employed, even the removal of one or both, proves futile.

The terms "neurotic or hysterical" applied to such symptoms frequently imply that a definite physical basis for the suffering has not been discovered. The more thoroughly the physical examination is carried out and the possibilities considered, the less will be heard of "neurotic or hysterical origin." A recent instance in the writer's experience serves as a useful illustration.

A young woman, who had suffered from chronic pain in the right iliac fossa, at times increased, was examined under anæsthesia at an important hospital. Nothing was detected, and she was discharged, being informed that the trouble was neurotic. As her pain continued and interfered with her liveli-

hood as a dressmaker she sought further advice. The pain and localized tenderness suggested some trouble in the region of the appendix, and on exploring the abdominal cavity a well-marked, right-angled kink of the appendix was discovered. Complete cure of the pain has resulted, since the appendix was removed.

Kinks of the appendix, produced by adherent bands attached to the tip or to portions of the appendicular wall, are exceedingly common in the female. They give rise to pain persisting and increasing at intervals often most marked before the onset of the menstrual flow. They do not cause "rigidity, elevation of temperature, or leucocytosis." Should pregnancy supervene, the pain may disappear, or, what is not uncommon, may increase so as to demand surgical treatment. No doubt the growth of the uterus altering the anatomical relations may "cause the pain to shift."

Chronic appendicitis in women is characterized by increased pain before the onset of menstruation, and physical examination may reveal some enlargement of the right ovary. Too often the ovary is blamed and removed only to find that the old pain persists. The change in the ovary is secondary, and of the nature of a chronic oedema, which proceeds to a natural cure when the appendix is excised.

Yet another common cause of "right sided pain" is delay in the passage of the intestinal contents. The cæcum may then be found filled with fæcal matter. The majority of such cases yield to medical treatment, but in the event of failure the appendicular region should be explored.

SYPHILIS IN THE DIFFERENTIAL DIAGNOSIS OF TUBERCULOSIS.

By A. SALUSBURY MACNALTY, M.A., M.D.

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THE purport of this communication is to call attention to certain manifestations of syphilis, which may be confounded, from time to time, with pulmonary and glandular tuberculosis.

The varieties of disease which it is proposed to consider from this point of view fall into two groups :—

A. Syphilis of the Lung.

B. Syphilitic Adenitis.

A. SYPHILIS OF THE LUNG AND PULMONARY TUBERCULOSIS.

Osler states that syphilis of the lung is a very rare disease. "In 2,800 post-mortems at the Johns Hopkins Hospital, there were 12 cases with syphilitic disease of the lungs ; in 8 of these the lesions were in congenital syphilis. In 11 cases there were definite gummata. Clinically, the presence of syphilis of the lung was suspected in these cases."

This view as to the rarity of the disease is supported by Sir J. Kingston Fowler and by such writers as Bandelier and Roepke, all of whom base their opinion on post-mortem evidence.

On the other hand, many authorities incline to the view that syphilis of the lung often escapes recognition. This may very readily be so, for—

a. Syphilis of the lung is liable to be confounded with pulmonary tuberculosis.

b. A large proportion of cases of all disease in Great Britain do not come to post-mortem.

c. If other syphilitic lesions are exhibited, the pulmonary condition will be treated unawares or alternatively

will be diagnosed as pulmonary tuberculosis complicating syphilis. (The consequent improvement in the pulmonary lesion will be ascribed to successful tuberculosis treatment, carried out simultaneously.)

d. In the non-gummatous variety of pulmonary syphilis at autopsy there are no characteristic lesions, and the condition will be classified under such a general term as "fibrosis of the lung."

Excluding congenital pulmonary syphilis, "the white pneumonia of the fœtus," pulmonary syphilis occurs in two forms :—

1. *The gummatous form.*—The lesion in this variety assumes the form of definite gummata of varying size, of a yellowish-gray colour, caseous, embedded in tough connective tissue, and more numerous towards the root of the lung. With this appearance, areas of pneumonic consolidation may be associated. If extensive gummata are present in the lung, there is a possibility that they may undergo great caseation and may break down, giving rise to cavity formation.

Osler records a case of this rare type, the only one that has fallen under his observation.

It was that of a man, aged 27, who had had for a year cough and blood-stained sputum; he died of a severe hæmoptysis. Tubercle bacilli were never found in the sputum. At the autopsy, both lungs displayed throughout extensive caseous gummata with a large amount of fibrosis. There was a cavity 3 by 5 cm. in diameter in the lower lobe of the right lung, on the wall of which a branch of the pulmonary artery was eroded. The whole clinical picture simulated pulmonary tuberculosis.

A presumably analogous case has fallen under my own observation :—

L. F., a married woman, aged 35, had a miscarriage three years previously. There was no history of a rash or sore throat. Since the miscarriage, she had never regained her strength, was troubled with a severe cough with expectoration and occasionally brought up small quantities of blood. She consulted a doctor, who informed her that she was suffering from consumption, and recommended treatment at a sanatorium. She underwent sanatorium treatment for a period of four months, with little relief to her symptoms. She was never febrile, except when undergoing a brief course of tuberculin, but she steadily lost weight, and was discharged from the sanatorium as a case of pulmonary tuberculosis on the downward grade. It should be noted that at no period were tubercle bacilli detected in the sputum. About June, 1913, she came under my care at the County of Essex Tuberculosis Dispensary. She was then

considerably emaciated; a large cavity was present in the upper lobe of the right lung: the right lung was uniformly dull to percussion; the left lower lobe was consolidated and patches of "softening" were present; rhonchi and scattered crepitations could be heard on auscultation throughout both lungs.

The patient's blood was examined by the Wassermann test, and proved positive. She was then put on a course of potassium iodide and mercury.

By October, 1913 her general condition had much improved. The troublesome cough had disappeared; she had no sputum, and had gained in weight; the upper lobe of the right lung was fibrosed, and slight dulness persisted at the base of the left lung. The Wassermann reaction was now negative.

Clinically, the patient would have passed for an arrested case of pulmonary tuberculosis.

II. *The pneumonic form.*—Virchow pointed out that cases displaying a chronic interstitial pneumonia, which begins at the root of the lung and passes along the bronchi and great vessels, are of syphilitic origin. In some examples, gummata are associated with the fibroid lesions. As a rule, only one lobe or portion of a lobe is involved.

Syphilitic visceral lesions may be present in addition, or the subject may have a definite history of venereal disease.

With regard to the clinical picture presented by syphilis of the lung, from what has been said already respecting the pathology of the disease, it will be obvious that no characteristic features are present, and that the physical signs elicited may be quite comparable to those displayed by a case of chronic pulmonary tuberculosis, associated with some degree of fibrosis.

It is stated that dulness to percussion usually precedes the appearance of catarrhal and adventitious signs, while pyrexia and hæmoptysis are not often present.

It is in cases presenting anomalous features such as these, and in which there is a persistent absence of tubercle bacilli in the sputum, that the question of syphilis of the lung has to be tentatively considered by the clinician.

In this connection, a paper, published in the *Wiener klinische Wochenschrift* (1914), by Dr. Kraus, is of interest.

The writer is in charge of a private sanatorium for pulmonary tuberculosis. In the course of one year, among the small number of patients under his care he detected four

cases, admitted like others with the diagnosis of pulmonary tuberculosis, in whom the Wassermann reaction was positive.

The salient feature in each case was a relapsing pyrexia. The pulmonary symptoms and physical signs were slight, and tubercle bacilli were absent from the sputum.

When anti-syphilitic treatment was given, after an initial sharp rise there was a rapid and persistent return to the normal temperature.

I have no desire to emphasize the frequency of syphilis of the lung, but it is quite possible that the disease may occasionally be overlooked for the mere reason that, being a *rara avis*, it never crosses the physician's mental horizon. We now possess in the Wassermann reaction a valuable means of diagnosis, and the test, as yet, has been little employed in obscure cases of pulmonary disease.

A marked syphilitic history and the presence of luetic stigmata will be valuable auxiliaries in the first stage of the investigation of a suspected case.

When other syphilitic lesions are present, the diagnosis is arrived at more readily.

The following is a case in point :—

F. W., male, aged 42, was admitted to the Brompton Hospital for Consumption under the care of Dr. Wethered ; through his courtesy, I am enabled to publish the case.

The patient had had a penile chancre 20 years previously which was untreated. He had suffered from malaria and rheumatic fever in India.

On admission, he complained of cough and frequent expectoration. His private doctor had sent him to hospital with the diagnosis of chronic pulmonary tuberculosis. No tubercle bacilli were found in the sputum (repeated examinations). The physical signs were confined to the upper lobe of the right lung. The note here was dull to percussion ; on auscultation, the breath-sounds were bronchial in character, and whispering pectoriloquy was elicited over the dull area.

The patient had a gumma of the right testicle.

In spite of the pronounced pulmonary physical signs, the temperature was normal throughout the period of observation. He was placed on anti-syphilitic treatment (mercury and potassium iodide).

The cough and expectoration ceased ; the abnormal signs in the chest disappeared ; the right testicle was little larger than the left when the patient left the hospital at the end of three months' treatment.

For six months subsequently, the patient attended the outpatient department of the hospital. The improvement persisted.

It is well known that a patient who has been or is the

victim of syphilis has a predisposition to infection by the tubercle bacillus. Further, in the differential diagnosis the possibility that a patient with pulmonary tuberculosis may acquire syphilis must be borne in mind. These mixed cases are exceedingly interesting, but their full elucidation still awaits further clinical and pathological investigation.

B.—SYPHILITIC ADENITIS AND TUBERCULOUS ADENITIS.

The lymphatic glands may be affected in various ways in the successive stages of syphilis.

(*a*) In the primary stage, the lymphatic glands nearest to the primary sore become enlarged, hard, "shotty," and of approximately the size of an almond. They move freely under the skin. As a rule, unless the glands suppurate owing to the absorption of septic material from the primary lesion, this enlargement is painless.

It is stated that, with extra genital chancres, there is a greater degree of enlargement and infiltration than is the case with genital chancres (Rose and Carless).

(*b*) In the secondary stage, when there is a general infection of the body by means of the blood stream, the glands become hard and enlarged in various regions.

(*c*) In the tertiary stage, true gummata may appear in the glands, or a chain of lymphatic glands, may become enlarged and tender through the absorption of septic material from a broken-down gumma.

It is in the two latter stages that syphilitic adenitis may be confounded with tuberculosis of the glands. On clinical examination, alone, the differential diagnosis is often very difficult (Bandelier and Roepke).

In discussing this question, the remarks already made concerning the differentiation of pulmonary tuberculosis and pulmonary syphilis, in so far as they relate to history, other syphilitic lesions, and the Wassermann reaction are equally applicable.

That the necessity for making the differential diagnosis arises from time to time is borne out by the following illustrative case :—

H. D., aged 46, a draper's assistant, came under my care in May 1913. He was a married man, and had four children. His wife had a mis-

carriage twelve years ago. He denied venereal disease or exposure to infection.

For the last five years he had suffered from "glands of the neck," which he had always been given to understand were of tuberculous origin. The glands had been operated upon at the local hospital on at least six occasions; they had always recurred, and he suffered much from the irritation and discharge from the open wounds in the neck.

Owing to the condition of the neck, the patient had been unable to follow his employment for the last two years. The diagnosis of tuberculosis had led him to look upon himself as a source of infection toothers, and he now lived in an outdoor shelter erected in his back garden. For the past six months he had been troubled with a bad leg. His medical attendant now sent him to me, thinking that he might derive benefit from a course of tuberculin. He was accustomed to attend at the hospital daily for dressings for the neck and leg.

On examination of the patient, numerous glands were palpable in both cervical triangles. Some of the glands were hard and "shotty," others softer in consistence; a good deal of periadenitis was present. On both sides of the neck, scars of old operations were visible; on the right side of the neck were two or three sinuses discharging thin pus; on the left side, two small sinuses were present in the neighbourhood of a puckered scar; the latter showed a distinct tendency to keloid formation.

Below this and extending downwards towards the clavicle was an open, suppurating wound, the edges of which were apparently secondarily affected. The enlarged glands in the neighbourhood of this wound were red and angry looking. On the left tibia was situated a deep ulcer of serpiginous outline, which showed slight tendency to scar formation. A foetid discharge oozed from the ulcer. A few small areas of brown pigmentation were present on both legs.

I came to the conclusion that the ulcer on the leg was of syphilitic ætiology, at all events, and that, in view of the scant success of surgical and hygienic treatment, the adenitis was as well, probably, of luetic origin. The Wassermann reaction proved to be positive. Soon after being placed on anti-syphilitic treatment (potassium iodide and mercury), the patient began to improve.

When I last saw him, in January, 1914, the periadenitis had disappeared, and the sinuses in both cervical triangles, together with the open wound on the left side of the neck, had healed completely. Only a few small glands, about the size of a pea, were palpable, whilst a long scar in the leg remained as a vestige of the ulcer. The patient had gained considerably in weight, and intended shortly to resume his occupation.

The course of treatment was attended with little inconvenience to the patient. The mixture of potassium iodide and mercury—the iodide being gradually increased in the customary manner—was given in fortnightly stages with weekly intermissions. If proceeded with for a longer period than a fortnight, an iodide rash made its appearance on the forehead.

In July, 1913, a syphilitic lesion, presumably activated by treatment, appeared on the back, in the form of a small ulcer over the situation of the second and third lumbar vertebræ; this healed completely, as

treatment was persisted in.

In November, 1913, Dr. Fildes, of the London Hospital, found the Wassermann reaction to be negative.

In this particular case, the presence of the ulcer on the leg was of considerable aid in arriving at a correct diagnosis. It was possible, however, as the history shows, for the case to be mistaken for tuberculous adenitis on several occasions, and in view of the possibility of such error the case seemed worthy of record.

It is conceivable that the clinician may meet with other examples of syphilitic adenitis simulating tuberculous adenitis; in these, no other syphilitic lesions may be present, and here again, as in the case of syphilis of the lung, the correct diagnosis may offer difficulties.

ANEURYSM OF THORACIC AORTA SIMULATING PULMONARY TUBERCULOSIS.

The following unusual case relates to another form of disease of syphilitic origin, which simulated pulmonary tuberculosis:—

It is noted here for the sake of completeness, though it has little practical bearing on the general question of the differential diagnosis of syphilis and tuberculosis. I am indebted to Dr. Hector Mackenzie for permission to publish the case.

T. B., male, aged 37, a soldier, was admitted to Brompton Consumption Hospital, under the care of Dr. Hector Mackenzie in June, 1910.

For the previous two months, he had complained of cough and shortness of breath. A fortnight before his admission, he had a brisk hæmoptysis, and continued to expectorate coloured sputum. A further small hæmyptysis occurred on his way to the hospital. The physical signs, on admission, suggested consolidation of the upper lobe of the left lung—dulness to percussion, and bronchial breath-sounds accompanied by diffuse crepitations were present over this pulmonary region.

The patient had a violent hæmoptysis, and died on the day after his admission to the hospital.

At the post-mortem, the following condition was found in the thoracic cavity:—

Immediately opposite the origin of the left subclavian artery, a sacculated aneurysm, arising from the inferior aspect of the thoracic aorta, was present. This had penetrated into the upper lobe of the left lung, and eventually had ruptured into the left pleural cavity: the latter contained 50 ounces of blood clot.

Extensive atheroma of the thoracic aorta was present. There was no evidence of pulmonary tuberculosis, the physical signs and symptoms that

obtained during life being evidently dependent upon the presence of the leaking aneurysm.

CONCLUSIONS.

1. Syphilitic affections of the lung or glands may simulate tuberculous disease of the lung or glands.
2. Syphilis of the lung is stated by many authorities to be a disease of great rarity.
3. Others advance the opinion that syphilis of the lung occurs more frequently than has been supposed, but that, as a rule, it is confounded with pulmonary tuberculosis.
4. The possibility of error is augmented by the fact that syphilis and tuberculosis may occur at the same time in the same subject.
5. Certain cases of syphilis of the lung and syphilis of the glands have been recorded in illustration of the confusion with cases of tuberculosis.

CEREBRO-SPINAL FEVER.

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DURING my residence as House Physician and Resident Medical Officer under Dr. Robb in the Belfast City Fever Hospital, from 1906 to 1908, I had the opportunity of observing over 300 cases of cerebro-spinal fever, and this article is mainly based on the notes of these cases.

The first case I saw was on December 29, 1906, when three children, all from one house, were admitted into hospital with the most alarming symptoms, two being wildly maniacal. Dr. Robb diagnosed cerebro-spinal fever, and this was confirmed by post-mortem examination, and the recovery of the meningococcus from the spinal and ventricular fluid by W. J. Wilson. Three days later, two more children from the same house were admitted with the same disease. Of these five, three recovered and two died.

No more cases were admitted until January 24, 1907, when three children, also of one family, were admitted with the disease; of these, two died and one recovered. The one that recovered had a very mild attack, and if the other children had not been ill, most likely the disease would have been overlooked. The only symptoms in this case on admission were: temperature 100°, general glandular enlargement, enlargement of the parotid, absent knee-jerks, and some endocarditis. Two members of this family died outside hospital. The post-mortem examinations were made by Professor Symmers, and the meningococcus was isolated. Another member of the same family was admitted on January 31, and died. In all, six members of this family were affected, and five died.

After January 24, cases came in rapidly, and until I left, in May, 1908, cases were still being admitted. Some of the patients were wildly delirious, and the sudden onset of this delirium is one of the marked features of

the disease. In one case, death thus occurred 7 hours after the onset. On the other hand, several cases were of so mild a character, that the word cerebro-spinal seemed a misnomer; this feature of the disease is, I believe, of great importance, when we come to study the manner in which cerebro-spinal fever is spread.

The disease was first recognized by Vieusseaux, at Geneva, in 1805; since then there have been numerous epidemics, which Hirsch divides into four periods.

During the *first* period, 1805 to 1830, North America was chiefly affected. In Europe, outbreaks occurred at Grenoble and Paris, 1814; Metz, 1815; Geneva, 1815; Sunderland, 1830.

In the *second* period, 1837 to 1850, Europe was largely affected, the epidemics being specially severe in France. Italy, Denmark, Iceland, Algiers, and Great Britain and Ireland had epidemics, and at the end of this period there was a widespread epidemic in the south-western States of the U.S.A.; in Ireland, Dublin, Bray, and Belfast had very severe outbreaks.

In the *third* period, 1854 to 1874, Germany, Sweden, and Russia were chiefly affected, and there were outbreaks in Carolina and New York. In Ireland, in 1865, 1866, and 1867, Dublin and Belfast were again the seats of the disease.

In the *fourth* period, 1876 to the present time, there were slight outbreaks in the north-eastern States of the U.S.A.; some in Europe; and some in England—in the Midlands (1876); Dundee (1877–8); in Dublin (1885-6) among the well-to-do. In 1900, in Dublin (3); in New York, a severe epidemic in 1905; in Glasgow 1906, and Belfast 1906, 1907, and 1908.

GENERAL FEATURES.

Influence of Climate and Race.—It appears to occur between 45° and 30° N. in the western hemisphere, and between 63° and 30° N. in the eastern. It seems to have no special predilection for race or sex. It is most common when there is overcrowding.

The influence of cold, heat, and moisture, according to some, is not very great. According to Robertson, of Leith, the disease was most prevalent in cold, dry, dusty weather. At Purdysburn,

we got more cases during the cold weather.

Age.—Hirsch in 1,267 cases found 71 per cent. under 15 years, 26 per cent. between 15 and 40 years, and 3 per cent. over 40 years. The Gouverneur series showed under 1 year 9 per cent.; 1 to 5 years, 38 per cent. (Taves). In the Purdysburn series, out of 255 cases there were:—

Under 1 year	5 per cent.
1–5 years	23·9 „
5–10 „	26 „
10–20 „	23·9 „
21–30 „	12·1 „
31–40 „	7·4 „
Over 40 years	1·1 „

In camp and garrison, the age incidence would be higher. In the Italian epidemic (1840–5) adults were mainly affected. In Billings's series, out of 424 cases 16 per cent. were under 1 year. In the Purdysburn cases, about 79 per cent. were under 20 years of age. Generally speaking, therefore, the disease is most often met with from infancy to adult life.

Predisposition and Immunity.—While infancy and early adult life apparently predispose, it is difficult to be dogmatic on other points. The following facts are suggestive. Doctors and nurses, as a rule, escape infection. At Purdysburn, the doctors and nurses were exposed in every way to infection, for the patients were wildly delirious in many cases and had to be restrained. Patients have vomited, coughed, and spat in my face while attending to them.* There was, however, excellent ventilation there, and personal and other disinfection was thorough. Many people not affected by the disease act as carriers. There must be, therefore, a certain amount of individual immunity. With regard to immunity after having the disease, second attacks have been known to occur. There was one such in the Purdysburn series. Relapse is common.

Period of Incubation.—Taves, quoting Bolduan and Goodwin, gives 34 instances in which there was an interval between removal or death and the onset of disease. In

* Every opportunity and encouragement were given to the staff to go out and get as much fresh air as possible.

14 of these cases the interval was from one to two days. They give an instance which points strongly to three days being the incubation period.

At Purdysburn, the intervals were, as far as I have noted, one of three days, one of four days, one of six days, and one of seven days. In the case of one patient I know of, she was exposed a fortnight before the onset, and then, later, for four days previous to the onset she was attending a patient with the disease.

SYMPTOMS AND SIGNS OF THE DISEASE.

The mode of onset is very typical, and is of importance in diagnosis from other diseases, such as typhoid or post-basic meningitis. The onset is very sudden, beginning with headache and vomiting, followed by stiffness of neck, back, and legs, the patients becoming rapidly unconscious and comatose or wildly delirious. Of the 300 cases I observed, 90 per cent. began in this manner, with headache and vomiting; delirium or unconsciousness was present in about 80 per cent. Pain in back and legs as well was complained of in nearly all the cases. Stiffness of the neck and Kernig's sign, as Robb states (B.M.A. 1907), were present in all except the very mild or very toxic cases. Billings found Kernig's sign and stiffness of neck in 85 per cent. of his cases, Ker in 70 per cent. In Billings's series, headache was present in 238 out of 365 cases. Taves found headache in 90 per cent. Vomiting was present in 336 out of Billings's 365 cases, and Taves found it in 86 per cent. Convulsions were frequent in the Purdysburn cases, especially when the disease was fulminant. Billings found convulsions in 245 of his cases.

Vomiting becomes a serious factor after the acute symptoms have subsided, and is usually accompanied by headache; chronic hydrocephalus is the most probable cause. In one case of this sort at Purdysburn, hydrocephalus was found marked on post-mortem. In six cases out of 75 in which special inquiry was made, diarrhœa was present before the onset of the disease in young children.

Temperature.—There was great variation in the Purdysburn cases, and sometimes this variation was very rapid. In some cases, there was a periodic rise at a certain time of the day. In several cases, there was a high morning and a low

evening temperature. In 75 cases, in which I have closely analysed this symptom, the lowest temperature was 96°, and the highest 107·6° F. In toxic cases, the temperature was most frequently low. The temperature, as Robb states, was of little value in diagnosis. In the ordinary case, the temperature was about 102° at the onset, and on the second or third day it fell to normal; secondary rises were frequent. In 75 cases alluded to above, the average variation of temperature was 3·9.

Pulse.—At Purdysburn, the cases showed great variation in the pulse rate, which frequently did not rise with the temperature. A temperature of 103° with a pulse of 60 was, as Robb states, frequently observed. In the most rapidly fatal cases, the pulse was slow, full, and delayed, and in these cases there was a general cyanosis and bluish mottling on the skin. One point I noticed was that the pulse, just up to death, was of good volume and tension, and not unduly frequent, while the respirations were very rapid, râles and rhonchi being heard all over the lungs, and there was profuse discharge from the nose and throat.

Rashes.—One may say, not inaptly, that cerebro-spinal fever is called "spotted fever" because there are no spots, for in the majority of cases there is no characteristic rash. Allbutt classifies the rashes as petechial, erythematous. urticarial, vesicular, bullous, rose spots, herpetic, and purpuric. Of these, the most typical of the disease are the last two. In Purdysburn, the rashes were most frequent in the first lot of cases admitted. Rashes in the first 75 cases were: petechial, 12; uticarial, 2; erythematous, 6; purpuric, 24; herpetic, 19. Rashes in first 255: herpetic, 103; various, 66.

One must bear in mind that petechial rashes are common in many badly cared-for children. In 60 cases (Huber) this rash was present in 14 cases. Billings states they are quite as numerous as herpes. Taves states they occur earlier in the disease; in the Purdysburn cases, this was not the case.

Herpes.—In the Purdysburn cases, it was most common about the lips, but was frequently on the chin, cheeks, and forehead; it was present less frequently on almost every part of the body, fingers, toes, scalp, arms, trunk, and legs. Tourdes observed it in two-thirds of his cases.

It generally comes out before the fifth day, and most fre-

quently on the fourth day. In Taves's cases, it was present in 25 out of 105. Huber and Monroe found it in 16 out of 60 cases. With regard to the Purdysburn cases, 69 out of the 183 deaths occurred before the fourth day, when herpes generally appears.

Urticaria.—Urticaria was occasionally noticed at Purdysburn ; it was more frequent in cases which received serum.

Erythema.—Erythema was in one case as marked as in scarlet fever.

Purpuric Rashes.—In Purdysburn these were more frequent in the earlier cases admitted. There were various forms. In the majority of cases, there were red spots, evidently due to continuous hæmorrhage, which varied in shape, did not fade on pressure, and were a brighter red than typhus spots ; in some cases, there were large blotches of hæmorrhage, and in one case the portion of the body covered by the blotches was larger than the uncovered. The spots were quite different to typhus and typhoid spots. In two cases, the spots were bluish purple and slightly raised, irregular in shape, and distributed generally over the body ; they varied in size from a grain of barley to a bean. With regard to this purpuric rash, similar spots were observed, in most of the post-mortems, on the peritoneal surface of the intestines, bladder, kidneys, on the heart, and occasionally on the pleura.

Desquamation.—This only occurred in two cases out of 255 ; it was quite definite and rather flakey in character. Orange colour of the palms was present in three cases out of the first 75 cases. *Tache cérébrale* was noticed in many of the cases.

Nervous Symptoms.—In addition to the delirium and the rigidity of the neck and legs mentioned previously, as well as the convulsions and unconsciousness, there are other nervous symptoms and signs. The *mental condition* is of interest. At times, a patient would be delirious, and then suddenly would become quite sensible and frequently witty, making humorous remarks much to the point. There seemed to be conditions of mental torpor followed by excitement. Frequently the delirium was so marked, that the patients had to be restrained ; one man took eight of us to move him from the ambulance to the bed, and he had to be chloroformed to

be taken off the stretcher. As many as nine patients, in a ward containing 11, have been under restraint at once in Purdysburn. Another point is the desire to get out of bed; this, in treating the disease, must never be lost sight of.

Motor Symptoms.—Rigidity of neck and legs has been mentioned, as well as convulsions and violence; opisthotonus occurs occasionally, and was observed in one Purdysburn case. Nystagmus was present in three out of the first 75 cases.

Sensory Symptoms.—With regard to sensation, there was marked hyperæsthesia, both physically and mentally; it was present practically in all cases. The headache which has been mentioned previously was at times unbearable, and often came on quite suddenly during the course of the disease, accompanied by vomiting.

Attitude.—A frequent position was to lie curled up in bed, with the knees almost touching the abdomen, the neck retracted, and the back arched; often, if conscious, the patient would draw the clothes up over the head, and resent any disturbance, sometimes using language one would not have expected.

Hydrocephalus.—This was present in a large number of children, who lived long enough; the bulging of the fontanelles was very marked in some, and this condition could be relieved for a while by lumbar puncture. It was a common cause of headache and vomiting, when the disease had lingered for some time. In one case, headache and vomiting were present off and on for months, till suddenly, one day, the patient had a very severe attack and died. Post-mortem, hydrocephalus was found, the ventricles of the brain being distended.

Circulatory System.—In toxic cases, the circulation was very sluggish, the skin being cyanotic, with bluish mottling in places, the pulse in these cases being slow, irregular, full, and "delayed." In the heart, the first sound was frequently muffled; definite endocarditis was present in seven out of 253 cases. Pericarditis was present in 11 cases.

Respiratory System.—Bronchitis was present in nearly all the acute cases, and definite pneumonia was present in 25 cases out of 255. Pleurisy was present in three cases. The respirations in the acute cases were very rapid, and the patient

appeared, in dying, to undergo a slow asphyxia.

Lymphatic System.—The glands were generally enlarged. The spleen was occasionally enlarged, especially in the typhoid type of the disease.

Urinary System.—The chief point to remember is the frequent occurrence of retention of urine. Vomiting may often be due to this. In a few cases, incontinence was present. In the cases examined for albumen, nothing beyond an ordinary febrile albuminuria was present.

Alimentary System.—Vomiting at the onset, and the later vomiting due to hydrocephalus, have been mentioned. It was a very troublesome symptom to treat; lumbar puncture sometimes gave relief. Diarrhœa was found in children. Constipation, though mentioned by some writers (Omerod in Allbutt's system), was not very common, but, when present, was very troublesome. Colicystitis was present in one case.

Special Senses.—Deafness was present in 14 out or 225 cases. It may be due to a purulent otitis media or to disease of the labyrinth. Deafness was not so marked a symptom in this epidemic as in many others, in which it has exceeded 50 per cent. of the cases.

In the nose, purulent rhinitis was frequent, and was present in 22 out of the first 75 cases. A curious point I noticed in fulminant cases was a peculiar aromatic odour, the exact cause of which was not obvious; in other words, you could smell a "spotty case" and diagnose accordingly. The following eye symptoms were present in 225 cases at Purdysburn:—Squint, 67; iritis, 10; keratitis, 6; blindness, 6; corneal ulcer, 3. Congestion of the conjunctiva was present in nearly all. Huber and Monroe found it in 60 per cent., and Randolph in 80 per cent. of their cases. With regard to the condition of the pupils, 31 out of the first 75 cases were dilated and 5 unequal.

Mouth and Throat.—A very foul condition of the mouth and throat was present in the large majority of cases. In the most acute, this was a dreadful symptom; froth and pus poured out from the mouths of some of these cases towards death, and, combined with purulent nasal discharges, the distressing breathing, and cyanotic colour, it was horrible to see a dying patient. Tonsillitis was noticed in some cases. In practically

all the cases, the tonsils and pharynx were congested; many cases were too violent to allow examination.

Emaciation.—This is a very characteristic symptom; the emaciation is terribly rapid, the flesh almost seeming to melt off some of the patients.

Some of the complications and sequelæ in the Purdysburn cases were:—

Herpes	103	Rash, various	66
Squint	67	Pneumonia	25
Facial paralysis	14	Paralysis of the arm	2
Hemiplegia	5	Paraplegia	2
Aphasia	5	Parotid (enlarged)	2
Endocarditis	7	Pleurisy	3
Pericarditis	11	Keratitis	6
Iritis	10	Corneal ulcer	3
Blind	6	Synovitis (suppurative)	3
Gangrene	4	Deafness	14

This table gives a good idea of the complications met with; in the various epidemics, the evidence of complications and sequelæ has varied considerably.

VARIETIES OF DISEASE.

Allbutt classifies them as: (1) simple, (2) malignant, (3) abortive, (4) intermittent. I observed the following types at Purdysburn:—(1) Acute fulminant and toxic, (2) ordinary, (3) chronic, (4) abortive, (5) mild, (6) typhoid, (7) purpuric, (8) intermittent. In the *British Medical Journal*, 1907, I reported examples of the fulminant type. No more terrible disease can be imagined. At one moment, you have an ordinary individual in health and vigour; in a few hours, he is wildly maniacal and convulsed, with rapidly progressing cyanosis and filthy discharge from the nose and throat. Many such cases were seen at Purdysburn. Two types of the disease, the typhoid and the purpuric, are worth special mention. With regard to the typhoid type, the rigidity is slight, there are headache, enlarged spleen, slightly distended abdomen, and a coated tongue; the pulse, as well, simulates typhoid. The onset, however, is generally more abrupt, and the temperature more irregular. An example of the purpuric type was a case in which the surface of the body covered with purpuric

blotches exceeded the clear skin ; the neck was scarcely rigid, and Kernig's sign was absent ; the duration of the disease was in this case 22 hours. The meningo-coccus was isolated from the blood-stained fluid obtained by lumbar puncture.

POST-MORTEM APPEARANCES.

The details of a post-mortem examination performed by Professor Symmers will give an excellent idea of the changes found in the cadaver. The duration of the disease in this case was given as 14 hours, so there was no time for the characteristic emaciation. The pus, frequently present in the sulci of the brain, was not found in this case. This exudation is more common at the base of the brain ; in several cases, the distribution of pus thickly covered the vertical and lateral surfaces. Another feature commonly found but not present in this case is congestion of, and purulent exudation in, the bronchi ; it was present at other post-mortems I saw. Stuart McDonald (*Pathology of Cerebro-Spinal Meningitis*) finds very similar changes to those mentioned by Symmers. For further details, reference can be made to Stuart McDonald, Symmers, and other observers.

The body was well nourished; lividity of the face, ears, back, and shoulders marked. Hundreds of small red spots over arms, chest, neck. back, flanks; four on the legs. The *thymus gland* was enlarged slightly, reddened, and had small petechial spots on it. The *heart* had a dozen petechiæ, chiefly on the posterior aspect, and a hæmorrhagic spot, 3 mm. by 5 mm., in area. The *lungs* had no petechiæ. The *stomach* was injected, and the vessels of the mucous membrane, especially near cardiac end, were distended. The small *intestines*: the duodenum, jejunum, and upper part of ileum were normal; as one approached the cæcum, the solitary follicles became progressively more numerous, more enlarged, and more visible, without reddening, until in lower 3 feet of ileum the mucous membrane was positively mammillated with swollen solitary follicles; the lowermost Peyer's patches showed considerable amount of lymphoid tissue. *Large intestine:* an enormous number of swollen solitary follicles, especially in the sigmoid flexure. The *liver* showed marked yellowish mottling. The *spleen* and *kidneys* were slightly hyperæmic. *Urinary bladder* showed congestion of capillaries. The *mesenteric glands* were enlarged. The *brain* was greatly congested throughout; the pia mater and arachnoid were saturated with pinkish fluid, which accumulated in small bullæ over the cerebellum; no pus was visible to the naked eye ; the ventricular fluid was turbid and stained pink. Lumbar puncture was done post-mortem, and clear fluid obtained, from which the diplococcus intracellularis meningitidis was isolated by Professor Symmers.

The wide distribution of the lesions will be noticed,

and the intestinal changes are specially important, as will be seen later on. The conditions met with *post-mortem* in any case vary in accordance with the severity or duration of the disease.

DIAGNOSIS.

This comes under two parts (1) *At the bedside*; (2) *In the Laboratory*.

(1) AT THE BEDSIDE.—The points on which to lay stress are the sudden onset with headache and vomiting, the rapid appearance of rigidity of the neck and Kernig's sign, followed in some cases by delirium and coma. This onset is typical of cerebro-spinal fever, distinguishing it from post-basic meningitis and other more common forms of meningitis, such as tuberculous, staphylococcal, typhoid, and pneumonic as well as from typhus fever. Apart from the onset, the appearance of herpes on the fourth day, and the character of the rash, if present, are valuable aids to diagnosis. In such diseases as typhoid, typhus, and pneumonia, other signs may be found.

The following diseases with meningeal symptoms may simulate the disease—typhoid pneumonia, acute anterior poliomyelitis, typhus tuberculous meningitis, post-basic meningitis, influenza, anthrax, malignant smallpox, diphtheria, and streptococcal meningitis; such conditions as ptomaine poisoning, or other toxic conditions may give rise to error as well. Let us consider them in the order named.

Typhoid.—It is sometimes very difficult to distinguish, but, generally speaking, the more gradual onset, the character of the stools, spots if present, and the temperature curve, are all guides. The Widal test cannot be relied on, for cerebro-spinal cases may give it. The most reliable test is lumbar puncture and isolation of the specific germ; the estimation of the opsonic index is of great help, the index being raised when meningococci are treated with serum of cerebro-spinal fever cases. In one case at Purdysburn, published in the *British Medical Journal*, the patient had marked symptoms of cerebro-spinal meningitis, rigid neck, Kernig's sign, herpes, delirium, and later on severe convulsions. The onset was sudden; ten days before admission, the patient was taken suddenly ill with headache, and on the following day with severe vomiting and delirium. On admission, the abdomen was

slightly tympanitic, and the spleen was palpable, but these signs had been observed previously in cerebro-spinal fever cases. The opsonic index, however, was estimated by Houston, but it was not raised.* Lumbar puncture was performed, and the bacillus isolated in pure culture. That typhoid frequently shows symptoms of meningitis is admitted, and, as Curschmann states, this symptom is more marked during epidemics of cerebro-spinal fever.

Pneumonia.—Primary pneumococcal meningitis, according to Osler. is rare ; ordinary pneumonia with cerebral symptoms is common. I saw such cases at Purdysburn, and when in the Belfast Union Fever Hospital, where sometimes they came in as typhoid. There is, as a rule, a preponderance of lung symptoms, with signs in the lungs, the pulse and respiration rates and the character of the temperature will help to distinguish, before lumbar puncture and the opsonic count settle the matter ; agglutination will help too.

Acute Anterior Poliomyelitis.—When the poliomyelitis is of the ordinary type, the different onset and the more marked paralysis will distinguish it from cerebro-spinal fever ; but when it is of the meningeal type, the diagnosis may be difficult, for there may be sudden onset with retraction of the neck and Kernig's sign in both. In these cases, lumbar puncture will settle the diagnosis.

Typhus Fever.—Meningitis is very rare in typhus according to Curschmann ; in forty cases I saw, it was present in none. Tremor is frequent, however, and may give rise to confusion, and so may the rash to anyone who has not seen either disease ; as they are both rare, mistakes might occur. The onset is not so sudden in typhus, and the rash is distinctive, whilst Kernig's sign is generally absent. Lumbar puncture and the opsonic count would clinch the matter, but the agglutination test cannot be relied upon.

Tuberculous Meningitis.—The onset is less sudden, and most likely other signs of tuberculous disease are present. The absence of some of the typical signs of cerebro-spinal fever will help, and if the tuberculin reaction is obtained and no meningococci are found in the cerebro-spinal fluid, especially if

* See O'Carrol and Purser, *Dublin Journal Medical Science*, 1912, for a similar case.

it is clear and free from pus, the diagnosis would be in favour of tubercle; an opsonic count with the meningococci would help as well. The two diseases may co-exist.

Post-Basic Meningitis.—Stuart McDonald and most observers still support the conclusion that this is a mild and chronic form of cerebro-spinal fever. Houston and Rankin, on the other hand, believe the two diseases to be distinct, on account of the negative result of post-basic meningitis cases to agglutination and opsonic tests. Post-basic meningitis has a much less sudden onset, and is more chronic; post-mortem examination (Stuart McDonald) shows that the disease affects the cerebro-spinal meninges almost entirely.

Influenza.—Meningitis may occur in influenza, and the following symptoms may suggest cerebro-spinal fever:—sudden onset, with headache and perhaps vomiting; pain in back and limbs, followed by stiffness of neck and legs; the appearance of squint, herpes, and various neuroses. The pulse may be low, and the temperature variable. One case at Purdysburn simulated cerebro-spinal fever. In influenza, the rigidity is scarcely so marked, and the wild delirium and coma of cerebro-spinal fever are not present. Lumbar puncture and the estimation of the opsonic index will most likely settle the diagnosis, if beyond the six days, for the opsonic test is not reliable before then. The acute symptoms in influenza pass off more rapidly.

Anthrax.—The presence of a pustule, the history of exposure to infection, the slower onset, and the absence of marked rigidity will help to distinguish. Lumbar puncture and the opsonic test will make certain. An interesting case of anthrax meningitis is described by Symmers and Wilson, in the *Journal of Pathology and Bacteriology*, 1909.

Malignant Smallpox.—The symptoms of smallpox during the initial stage often simulate cerebral meningitis more closely than any other disease. The sudden onset, headache, vomiting, and pain in back all mislead, and as meningitis may occur, one must be careful. The erythematous rash on the crural triangle, if present, will help, and so will the history. On the 4th day, the small-pox rash, or lumbar puncture if positive for meningococci will settle the diagnosis.

Diphtheria.—Diphtheria of a very toxic type may be mis-

taken for a toxic case of cerebro-spinal fever. Examination of the throat, the examination of a swab for the diphtheria bacillus, and lumbar puncture will clear up the case.

Streptococcal Meningitis.—Wilson describes five cases. One of his patients, McV., was under my care at Purdysburn, and the symptoms appeared like those of cerebro-spinal fever, the meningitis being marked. The post-mortem findings as well were like those in cerebro-spinal fever. A streptococcus belonging to the fæcalis group was isolated. These cases could not be distinguished from cerebro-spinal fever except by bacteriological methods. Wilson also describes a case, which I saw at Purdysburn, as being due to the micrococcus catarrhalis. Symmers and Wilson describe a case due to the bacillus enteritidis (Gaertner). Cases of food-poisoning may give rise to difficulty, for in very toxic cases of cerebro-spinal fever the rigidity may be absent. Lumbar puncture would settle the point.

(2) IN THE LABORATORY.—The chief methods of diagnosis are:—

(*a*) The cultivation of the meningococcus from the lumbar puncture fluid.
(*b*) The estimation of the opsonic index.
(*c*) The agglutination of the meningococcus by serum from the blood of patients suffering from the disease.
(*d*) Cultivation of the meningococcus from the blood.

(*a*) In 37 cases, Symmers and Wilson obtained the meningococcus in 22. Taves states that the meningococcus is demonstrable in about three-quarters of the cases. In performing lumbar puncture, it is best to use a needle of the size used in a Potain's aspirator. A point is taken, on the line drawn joining the summit of the iliac crests, about a quarter of an inch to one side of the mid-spinal line, and the needle plunged in, upwards, inwards, and forwards; it may strike bone, in which case the point of the needle is turned up or down, till it slips past. A large needle is best, for one can manipulate better with it, and the fluid flows out more freely. The skin, needle, and test tube for receiving the fluid must be sterilized, as well as the hands of the operator. Chloroform should be given. In a typical acute case, the fluid is turbid; in

more chronic cases, limpid. It is rarely necessary to use suction to draw off the fluid. About from ½ to 1 oz. of fluid is generally obtained, and this must be examined quickly, else the meningococcus may die.

(*b*) The estimation of the opsonic index is a useful test after the sixth day of the disease, and should always be made.

(*c*) The agglutination test is not so reliable, owing to the heterologous agglutinins present in the blood-serum of cerebro-spinal cases. Huntoon and Elser point out the care necessary in arranging and carrying out this test, and advise old cultures to be used. A curious point is, however, that the serum agglutinates, in very high dilutions, a bacillus isolated from Belfast tap water, the bacillus aquatalis alcaligenes; in 184 samples of serum of cerebro-spinal cases, there was a positive reaction with a dilution of 1 in 50 in 163 cases.

(*d*) In three out of 15 cases, examined by Symmers and Wilson, the meningococcus was recovered from the blood. Wilson and myself obtained the blood in the following way:—

The bend of the elbow was very carefully washed with carbolic soap and water, then with spirit, and lastly with a strong solution of mercuric iodide (1 in 500). A sterilized pad was then soaked in the iodide solution, and left on for several hours. The veins were then made prominent by applying a bandage above the elbow, and a sterilized serum needle was inserted into the most prominent vein; the blood was received directly into a flask containing sterilized peptone water.

DESCRIPTION OF MENINGOCOCCUS.

It is a micrococcus, according to Councilman, of about the same size as the ordinary pathogenic micrococci, and appears as a diplococcus, the two hemispheres being separated by an unstained interval. They are gonococcus-like in form, and mostly intra-cellular in the polymorphonuclear cells of the exudate; one cell may contain one or more diplococci. They take the ordinary stains, and are Gram-negative, but Stuart McDonald says they may be Gram-positive as well. The cultures are glistening grey in direct light, and greyish white in transmitted light. The growth is confined almost entirely

to the surface of a stab culture. The organism (Symmers and Wilson, June 22nd, 1907, *British Medical Journal*) does not peptonize gelatine, produces indol, forms acid from glucose and maltose but not from galactose, gas is never produced, grows well in media containing ascitic fluid, and lives at least a week on glycerine-agar, from two weeks to a month on ascitic bouillon, and from two weeks to two months in fluid sugar media.

TREATMENT.

Drugs are of little use, and are only palliative. Phenacetin is useful for headache, and morphia and opium when pain and insomnia need attention. Hosts of drugs were used at Purdysburn. Bismuth and soda is useful for vomiting. Hot baths are good for relaxing the rigidity (Robb at British Medical Association, 1907). Ice-caps to the head are of benefit. Some patients require to be catheterized, a difficult matter with a wildly-maniacal patient. Patients should always be very carefully examined for retention, even if urine is being passed. Nasal feeding is often required, and may be difficult. Saline enemata are valuable, especially when the patient is collapsed.

One method of treatment stands out above all for use in this disease, namely, the intraspinal injection of Flexner and Jobling serum. The serum is obtained by inoculating a horse with gradually increasing doses of cultures of the meningococcus, which have been heated to 60° for half an hour. Different strains of the diplococcus were used. Autolysate was injected as well. (For further details, *see* Flexner and Jobling's paper in the *Journal of Experimental Medicine*, January, 1908.) The serum is sent out in 15 c.c. bottles, and has to be kept in an ice-box. The following precautions are to be observed in treatment with the serum:—The serum must be injected at body temperature. An equivalent quantity of spinal fluid should be withdrawn if possible, but this is not always essential. The injection must be given slowly, especially when the amount of fluid withdrawn is small, and not more than 35 c.c. are given for one dose. The first injection must be given as early as possible, and, in bad cases, repeated in 48 hours. Afterwards, the dose can be regulated by the temperature and

other symptoms, or by the opsonic index. There is generally a fall in temperature.

The technique is as follows :—The patient is prepared as for lumbar puncture. A short length of rubber tubing is attached to the needle. The phials of serum are immersed in a basin of water at a temperature of 102° F. To the rubber tube, the barrel of a serum syringe is attached, and the serum is poured into it; it flows in gently, and often it is not necessary to use the plunger. When the requisite dose has been given, sterilized lint is strapped on over the wound. Chloroform should be given. The fluid withdrawn should always be examined; as the case improves, it becomes less turbid, whilst the meningococci gradually grow less in numbers.

A curious point has been remarked by Houston and Rankin, namely, that the cerebro-spinal fluid has a lower agglutinative and opsonic power than blood-serum from the same case (*British Medical Journal*, November 16th, 1907). Flexner recommends the leucocytes in the circulating blood to be counted. Flexner and Jobling have noticed remarkable reduction in numbers of the meningococci after injection, and state that they were degenerated, and had lost power of growth.

To inject the serum hypodermically seems to be of little value. One case at Purdysburn was tested with intraspinal and hypodermic injections; the latter had no observable effect, while the former had (Robb, *British Medical Journal*, 1908). Other cases received hypodermic injections, but no effect was produced.

Other serums used before Flexner and Jobling's were Kolle and Wassermann's, Burroughs Wellcome's, Ruppel's, and serum from other patients, but none had any observable effect. The first three were examined by Houston and Rankin, and their agglutinative and opsonic power was nil.

With regard to results, the death-rate without serum was over 70 per cent. for the first 255 cases in hospital. In the town, at the time we were using the serum in hospital, the death-rate for cases not treated with serum was 85·2 per cent., whilst that in hospital was 26·6 per cent. This is a very significant comparison, as pointed out by Robb.

Flexner and Jobling, in the 47 cases they first recorded (January, 1908), had a death-rate of 27·6 per cent. Dr. Robb stated ultimately that it worked out in Belfast at about 24

per cent.

In Flexner's final report (*Journal of Experimental Medicine*) on 1,300 cases treated with serum, he gives the death-rate as 30·9 per cent. In 200 cases in which the serum was given during the first three days, the death-rate was 18 per cent. He found the patients frequently recovered by crisis, that the complications and sequelæ were very greatly diminished, and the number of permanent defects among these serum-treated cases was small.

There is in these figures a decided improvement on the death-rate in untreated cases, and the results, as far as they go, are better than the early results with diphtheria antitoxin. From the clinical picture of treated cases, one could vouch for the beneficial effect of the serum, the drop in temperature, relief of headache and rigidity (there was at times a slight increase, followed by a great improvement in the symptoms), the toxic colour of the patients disappeared, and the spinal fluid became clearer. I have observed a return of consciousness five hours after injection in a fulminant case.

The first case treated was interesting, being an ordinary severe attack of the disease in an adult, a type of case previously rapidly fatal. The result was watched with great anxiety, and when, 35 hours later, he became conscious, and recovered after further injections, we felt we had a new power given us to cope with the epidemic. Further cases bore out the value of the treatment. In one very severe case with very thick pus, the spinal canal was washed out as well as possible with normal saline before injection, with very good results.

*The foregoing remarks leave no room for doubt about the efficacy of the serum. Consequently, when a doctor sees a case and suspects cerebro-spinal fever, he should, without any further delay, inject the serum after lumbar puncture. To hesitate is perhaps to lose a life, and to me appears criminal. There is nothing to be gained by waiting for the result of bacteriological diagnosis, for by the time that arrives the patient is either dead or permanently damaged. Flexner's results, in cases treated within the first three days, are 82 per

* The early administration of the serum is a point on which Dr. Robb, after long experience of its use, lays great stress. The case mentioned on this page and injected by him was one of (perhaps the first) the first cases treated by Flexner's serum in this country.

cent. cures, instead of 74 per cent. deaths when no serum has been given. If given at the onset or on the first day, it is extremely likely that nearly every case, except the most toxic and fulminant, would be saved.

Vaccine Treatment.—Of this we had no experience at Purdysburn. The cerebro-spinal fluid of the patient, or cultures from it, may be used. This treatment would very probably be beneficial in helping serum treatment in chronic cases; an autogenous vaccine might be used, if the disease became chronic. Vaccine could similarly be prepared for carriers and mild cases, and used as a prophylactic for those exposed to infection.

PROGNOSIS.

This depends on the severity of the case, the virulence of the epidemic, the age of the patient, those under one year having less chance of recovery than those above that age. At Purdysburn the following table will give an idea of the influence of age:—

	Total.	Died.	Recovered.
Under 1 year - - -	13	12	1
From 1–5 years - - -	61	49	12
„ 6–10 „ - - -	67	46	21
„ 10–20 „ - - -	61	36	25
„ 20–30 „ - - -	31	23	8
„ 30–40 „ - - -	19	16	3
Over 40 years - - -	3	1	2

It will be seen that out of 74 children under 5 years, 61 died, and this agrees with the finding of Hirsch (*see* "Allbutt's System of Medicine")* that children mostly die; adults between 20 and 40 years, according to the above table, had a high death rate.

The duration of the disease is generally under eight days. 54 per cent. of the Purdysburn series dying within that time. Some cases linger very long; 21 cases at Purdysburn lingered for over eight weeks, one dying over 16 weeks from the onset. In the later stages, there is always the risk of hydrocephalus, and of progressive and profound emaciation.

Sudden death is common, even when convalescence is well

* In Flexner's final report the marked and beneficial effect of his serum is pointed out in the case of young children.

advanced, sudden cardiac failure or cerebral pressure being the cause. Several cases died thus. The prognosis must, therefore, be very guarded. If the serum is given, from what I have seen of its advantages, the outlook is very much better if it is given early, within 24 to 48 hours.

Convalescence is very slow sometimes, for headache and vomiting remain troublesome. It is a disease characterized, if one may use a paradox, by the suddenness and slowness of its termination. This is true. I have seen cases lasting months, and others almost stricken down dead.

Relapse may occur, though it is rare ; the various complications have been noted previously.

Sequelæ.—The principal in 255 cases at Purdysburn were :—Deaf, 14 ; blind, 6 ; paraplegia, 2 ; hemiplegia, 5 ; one case slightly affected mentally. Deafness and some forms of paralysis and blindness are the most frequent sequelæ. Some cases of paralysis and some of deafness improved before being discharged. In some cases there remains a tendency to severe headaches, and cardiac weakness. The latter may cause sudden death ; this occurred in two cases after discharge. The severe headaches were most probably due to slight hydrocephalus. In a table previously given will be seen the principal complications and sequelæ.

In Flexner's 1,300 cases treated by serum, the sequelæ were greatly diminished, and one cannot insist too strongly on the early injection of serum to prevent permanent defects following an attack of the disease.

COMMUNICABILITY AND MODE OF INFECTION.

Here we are not on very sure ground, and one must be cautious about jumping to conclusions. If some of the arguments in what follows are strained, let it be an excuse that we must have some theory to work on, and that one sometimes feels a thing is true without being able to express it adequately. With regard to the communicability of the disease, the viability of the meningococcus is important.

Viability.—According to Elser and Huntoon, recently isolated strains die out rapidly, and require early removal to fresh culture media. Symmers and Wilson recommend daily planting out ; in new strains later on, once every week

or two weeks is sufficient. It is important to prevent the culture media from drying (Elser and Huntoon). Old strains on ascitic agar have lived for 333 days.

Temperature.—von Lingelsheim (Elser and Huntoon) found 10 minutes at 60° C. destroy the organisms, but they resisted 45° moist heat for 3 hours. He adds that they die in 5 days at room temperature. Huntoon and Elser say they may survive 4 weeks at a room temperature of 25–26°, but none survive an ice-box temperature for 1 week.

Sunlight.—In diffuse daylight, none live after 8 days; in direct sunlight, 8 hours kill (Elser and Huntoon). von Lingelsheim states that from 4–8 hours, and Kutscher from 8–12 hours in direct sunlight are fatal.

Viability in Animals.—Young guinea pigs, mice, rabbits, and monkeys are generally used in experiments. Growth is feeble apart from the body, according to these authorities, and Stuart McDonald holds similar views.

Meningococci Carriers.—According to von Lingelsheim (Huntoon and Elser), meningococci are present in 93·8 per cent. of the throats of persons suffering from the disease, and according to Flügge, it disappears from the naso-pharynx after the fifth day of the disease. In several cases at Purdysburn, in which swabs were taken by Professor Symmers, meningococci were not found; these cases were past the fifth day. In several swabs which I took, and on Petri plates which I exposed to the breath of the patients, no meningococci also could be found by Professor Symmers; these cases were just past the fifth day. Farrand, quoted by Stuart McDonald, found that 23 per cent. of healthy persons, who had been exposed to infection, carried meningococci in their throats; 635 cases were examined. Fraser and Comrie (Ker's Paper), Jehle (Stuart McDonald), Albrect, Ghon, Weichselbaum, von Lingelsheim, Collins, Kolle and Wassermann, Osterman, etc. (Huntoon and Elser) all found meningococci in the throats of healthy persons exposed to infection. Comrie and Fraser found meningococci in Petri plates exposed in an engine-room, in which five fathers of infected children worked (Ker's Paper). Flügge estimates that the carriers are 10–20 times more numerous than the cases of disease. Kutscher has found meningococci present in four cases apart from epidemics.

Such occurrences are rare according to Kolle and Wassermann and von Lingelsheim, who examined over a hundred cases. In certain individuals, Weichselbaum and Flügge suggest that once the meningitis is established in the naso-pharynx, it is permanent.

These facts explain how it is that preventive measures, directed to the patient and his immediate surroundings, are useless alone (Elser and Huntoon). An instance of how the infection is spread in the above manner was that of the man employed in a dispensary, at which relatives and friends of people who had died of cerebro-spinal fever went to register death; he became infected, and died. In this connection, we may mention that the mild cases without definite meningitis, of which there have been several at Purdysburn, are a serious factor, too, in the spread of the disease. We can then have good grounds for believing that the infection is spread by non-infected persons who carry meningococci in their respiratory passages, and also by unrecognized mild cases, as well as by those who are severely affected.

Evidence has been found by many observers in the present epidemic (1915) of apparently healthy persons being carriers, and that the disease is spread by such persons can be regarded as pretty well proved.

Some observers have placed the percentage of contacts who act as carriers as high as 70 per cent. I would like to point out as well that vermin, such as fleas, lice, etc., probably spread the disease. Many of the petechial rashes observed could have been produced by pediculi, and many I saw were thus bitten. Typhus fever is spread by lice, and there are points of resemblance between these two diseases. Both are more common where there is overcrowding, and in cold weather; whilst, generally speaking, both are sudden in onset. In both there is evidence of bites of vermin. (Undoubtedly, however, the infection in both can be spread through the upper respiratory passages.)

I think, then, that the probability of vermin spreading the infection must not be overlooked. In Purdysburn, the patients were bathed on admission, the clothes disinfected, and I think this helped to prevent the staff becoming infected. In the army, I cannot too strongly urge that all clothes and belong-

ings should at once be disinfected by steam, and the soldiers given a fresh outfit after a bath in an effective disinfectant solution, *e.g.* kerol, cyllin, izal, etc.

Portal of Entry into the Human Body.—From the fact that the base of the brain, as well as the spinal cord, is most affected, it might seem possible that the infection generally spreads from the nose and throat directly by the lymphatics to the brain; for, as had been shown by Schwalbe, Kay and Retzius, Stuart McDonald, and other workers, the lymphatics of the nasal mucous membrane can be injected from the cranial cavity. On the other hand, Flexner in early experiments has shown that, in the case of monkeys after a spinal injection of meningococci, identical organisms were demonstrated in the nasal section of the infected animals. Another point against the view of infection spreading in the first instance from the naso-pharynx is the fact that the anterior part of the brain is not most affected.

Allan and Dun, quoted by Stuart McDonald, in a carefully reported case of fulminating cerebro-spinal fever, examined the cribiform plate and olfactory tract. They found that the olfactory epithelium gave no evidence of acute inflammatory change, and, though some of the lymphatic spaces passing through the foramen of the cribiform showed leucocytic infiltration, it was evident that this was quite as likely due to the spread from within as to the spread from without. McDonald goes on to say that he has not found any pathological evidence to show that the spread does take place from the nasal passages.

Besides this, Fowler (Ker in THE PRACTITIONER, 1908) states that the cord lesion is of older date than that of the brain. Greenfield has taught the same (Stuart McDonald) in regard to tuberculous meningitis, in which disease he believes the meningitis is not infrequently due to a lymphatic spread of the disease from the thorax or abdomen along the nerve routes to the lymphatics of the cord and thence to the brain. This would explain the basal exudate. Flexner has shown that the virus of poliomyelitis can be spread in this way.

Huntoon and Elser experimented on puppies by trephining well forward, so as to make the cribiform plate accessible. Subdural and intra-nasal injections of cultures of meningococci

were given. Cultures taken after the lapse of 2, 4, 6, and 24 hours failed to reveal meningococci in either locality. However, this experiment is deprived of real value, for the animals remained perfectly well. Westenhoefler has shown that, although the hypophyseal gland is involved, the suppuration is confined to the superior and lateral surfaces. Huntoon and Elser have, in two instances, made cross-sections of the hypophysis and sphenoid bone, but failed to reveal any evidence in favour of a direct extension through this portion of the base of the skull. Westenhoeffer has further proved (Huntoon and Elser) that the lymphatics at the base of skull show no evidence of invasion along these channels. The facts quoted, therefore, are against the view of a direct extension of the infection directly from the nose, throat and pharynx to the brain. It is probable that infection may occur this way, although it is not the most common route.

Other Portals of Entry.—We have the abdominal route, *via* Peyer's patches, solitary follicles, mesenteric glands, and perineural lymphatics to the cord. There are many points which make it possible, if not probable, that the meningococci reach the system by the abdominal route.

First of all, some premonitory diarrhœa has been noticed in patients suffering from cerebro-spinal fever by Lees and Barlow (Ker). At Purdysburn, on closely questioning the parents of children affected by the disease, I was able to find a history of previous diarrhœa in some cases. The early loss of the abdominal reflex, mentioned by Ker, points to the early involvement of the lower dorsal cord. Some cases mentioned by Stuart McDonald are very suggestive. In one death was due to general toxæmia from acute gastro-enteritis, but no meningococci were found; yet in the case of an elder brother, they were present.

If these cases are compared with those I published in the *British Medical Journal*, 1907, we see it is quite possible for a child suffering from cerebro-spinal fever to die of what is, to all intents and purposes, an acute toxæmia with little or no meningitis observable clinically.

In all these cases, the gastro-intestinal lesions were marked post-mortem. In case 18 of Stuart McDonald, the symptoms were gastro-intestinal, and there was no suggestion

of meningitis. In this case, too, there was post-mortem evidence of gastro-enteritis and, what is of importance as well, no signs of meningitis. In the mesenteric glands, what Stuart McDonald believes were meningococci were found. Meningococci, as far as I am aware, have not been found in the mesenteric glands.

Symmers, in the Belfast Hospital, found marked intestinal lesions in the case previously mentioned and in many others; to him the abdominal route seemed probable. The prevalence of acute gastro-intestinal toxæmia during epidemics of cerebro-spinal meningitis is reported by Stuart McDonald. May not this be cerebro-spinal fever?

With regard to the route of the infection in some other forms of meningitis, is not the origin of the meningitis in typhoid fever intestinal? Marked meningitis may be present, too, as in the case admitted to Purdysburn mentioned previously. Moreover, a certain amount of meningitis is fairly common in typhoid. There are marked changes in the intestine, in Peyer's patches, the solitary follicles, and the mesenteric glands. In tuberculous meningitis, it is possible that the bacillus may enter the system by the abdominal route, and it is extremely probable that the abdominal route plays a very important part in tuberculous affections of childhood.

Some interesting cases, published by Wilson in the *Lancet*, December, 1907, on streptococcal meningitis, may be mentioned as well; in three of these, he states, the organism appeared to be derived from the intestine. In anterior poliomyelitis, Leiner and Weisner have shown that the virus can pass through the intestinal mucous membrane.

We see therefore that little more than gastro-enteritis may be present in cerebro-spinal fever; that the cause for this can be shown by post-mortem findings; and that in many cases with meningeal symptoms, the intestinal symptoms appear first.

In no case, that I have seen post-mortem, have there been signs beginning in the brain, without signs in the intestine; although, as we have seen, there may be intestinal signs without lesions in the brain.

The lesions in the cord are said by some observers to be

older than those in the brain. (*See* Barnes, *Interstate Med. Journal*, September, 1913, for intestinal symptoms occurring before spinal.)

If, therefore, the intestinal signs are common, and the first to occur, the infection may start there. Is this possible? I believe it is quite possible, and that, as meningococci are present in the naso-pharynx, the infection takes place by the secretions from there being swallowed by the patients. This theory would fit in with the facts of cases. Infection, therefore, I believe, can and does occur through the intestinal route.

Another method of entry is through the blood-stream. In support of this, Huntoon and Elser have produced symptoms typical of the disease by injecting the blood-stream of animals. Another point, according to some observers, is, that the meningococci have been found in the blood before lodging in the meninges (Solmon, Martine, Rhode, Marcovitch and Andrews, quoted by Huntoon and Elser). In these cases, however, the symptoms were more those of septicæmia than of cerebro-spinal fever. Huntoon and Elser, after examining 41 cases, found meningococci in 11, but they do not regard the results as satisfactory enough to furnish conclusive evidence in favour of hæmatogenous origin of the disease.

Symmers and Wilson found the meningococci in blood in three cases out of 15 cases examined; the blood was drawn aseptically by Wilson and myself into nutrient media from typical cerebro-spinal fever cases.

The alarming suddenness of the onset and the widespread lesions found post-mortem are, however, in favour of the blood being the portal of entry. In other forms of meningitis, in which organisms gain access to the meninges at some particular point, the onset is gradual. There is no reason for assuming that meningococci, if they gained access at a particular point, would act in any different way from streptococci or pneumococci. These are the views of Elser and Huntoon. Besides, if infection does occur directly from the naso-pharynx, why does it not take place more commonly in such diseases as scarlet fever, diphtheria, and acute tonsillitis?

If the infection gets into the circulating blood, there are

several methods of entry. One may be through puncture of the skin, by such means as infected vermin, and others are through the tonsils, upper respiratory tract, or alimentary canal; the last occurs in anterior-poliomyelitis, as shown by Leiner and Weisner. There is no reason why the system should be infected in any way differently than in such diseases as scarlet fever, diphtheria, and typhoid fever, from the nasal passages or the intestines.

Summing up, therefore, it seems possible that the primary infection is—

A. *In the throat, nose, and naso-pharynx, and that from there it is spread* —

(1) As in scarlet fever, influenza, etc., into the blood-stream, the whole system becoming infected in this way, but more particularly the meninges of the brain and spinal cord.

(2) Directly to the brain or spinal cord.

B. *From bites of vermin*, such as lice, fleas, etc.

C. *Through the intestine*, from swallowing infected sputum, or the house fly may spread it through food.

The first (A 1) appears to me to be the most common method of infection, though I believe infection often occurs by B. and C.

GENERAL CONCLUSIONS.

(1) Cerebro-spinal fever is an acute disease, in which the symptoms, while largely meningeal, are not always so; acute toxæmia may be produced from infection by meningococci. The careful examination, bacteriologically if possible, of patients suffering from acute toxæmia is therefore recommended, especially when cerebro-spinal fever is epidemic. It may possibly be found that the name cerebro-spinal, applied to the disease, is as misleading as the title "spotted fever." Some cases are so mild as almost to escape notice, and these cases should be sought for carefully.

(2) The infection is spread through the agency of the secretions of the upper respiratory tract of infected people,

and some persons act as carriers. Mild cases are a source of danger. The organism sometimes exists in the upper respiratory passages for long periods, as in diphtheria.

(3) In order to prevent the disease, isolation of contacts, as in typhus fever, should be done, and antiseptic treatment of the upper respiratory tract should be carried out thoroughly as well. The disinfection of bedding and clothing, and the confiscation of infected foodstuffs should be carried out. Mild cases and cases of acute toxæmia should be watched for carefully.

(4) The commonest portal of entry is through the upper respiratory tract, nose, naso-pharynx, and tonsils. These become infected in the first instance, and the infection passes thence to the blood, or, more rarely, directly to the brain and spinal canal. Possibly, the respiratory secretions are swallowed, and the infection may be spread through the intestines into the blood or spinal canal. Besides entry in this manner, it is highly probable that infection is spread by lice, fleas, and other vermin, the disease germs getting directly into the blood stream.

(5) The treatment by Flexner and Jobling's serum by spinal injection seems to warrant its use in all cases and as *early* as possible. The delay of an hour may make a considerable difference in the final issue of the case. If cerebro-spinal fever is suspected, the serum should be given without waiting for the result of bacteriological diagnosis; by the time the report arrives the patient may be dead.

(6) In the estimation of the opsonic index, we have a very useful and reliable means of confirming the diagnosis after the sixth day, and the agglutination test, although not free from errors owing to heterologous agglutination, is, in the hands of a skilled bacteriologist, a useful aid.

(7) As errors may occur, owing to the possibility of other forms of cerebro-spinal meningitis being confused with cerebro-spinal fever, lumbar puncture should always be done, and the fluid examined bacteriologically. All other methods of bacteriological diagnosis should be made use of.

PREVENTIVE MEASURES SUGGESTED.

(1) The swabbing and supervision of all contacts, who must apply antiseptics to the nose and throat, *e.g.*, glyco-

iodine, glyco-thymol co., chloros, etc.

(2) Immediate isolation of carriers and infected persons; thorough disinfection by steam of all their belongings and clothes; on admission to hospital, to have a thorough bath, all vermin being looked for and destroyed.

(3) All persons exposed to infection and suffering from colds or "sore throats," or having gastro-enteritis, to be kept under observation, and attempts made to isolate the meningococcus from their secretions. Patients suffering from acute toxæmia or sudden and severe "bronchitis" during an epidemic to be looked upon as cerebro-spinal fever cases until otherwise is proved.

(4) Abundance of fresh air for patients and contacts; for troops, open tents or huts built on the "open air" principle should be provided. Patients to be nursed in the open air, when the weather permits.

(5) Inspections for vermin among troops, and when found the soldier to be given a disinfectant bath and his clothes disinfected.

(6) All food exposed to infection should be destroyed, and carriers warned against swallowing their own sputum; this should be received in special receptacles and disinfected; nasal discharges should be received on rags which are burnt at once.

(7) An energetic search to be made for mild and "missed" cases.

(8) From the character of the infection, it seems probable that prophylactic vaccine would be of value.

(9) All sanitary authorities, in districts where the disease is present, should supply through their Health Departments antimeningococcic serum free to doctors, and keep a stock in hand ready for use.*

I am indebted to Dr. Robb, the Medical Superintendent, Purdysburn Fever Hospital, for permission to publish notes of the cases referred to, and also to Dr. W. James Wilson for his kind assistance with the material for this paper.

* Since writing the paper, I have received from Dr. Robb, a circular letter which is addressed to the Belfast doctors recommending the earliest possible notification to the Fever Hospitals of cases, so that Flexner's serum can be administered without delay. I strongly recommend a similar notification being issued to the medical profession in those districts where cerebro-spinal fever is prevalent.

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RECENT WORK ON CHILDREN'S DISEASES.

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PYLORIC STENOSIS.

THE question of the best form of treatment in the case of infantile pyloric stenosis nearly always arouses acute controversy. In a recent number of the *Journal of the American Medical Association*, there are two papers dealing with this subject; one by Emmett Holt, who adopts the view that, in a considerable number of sufferers, the operative procedures are unnecessary and form an added danger, while in a smaller number operative interference is necessary and should be undertaken early; the other by the surgeon, Downes, of New York, recording the results in 22 consecutive cases.

Holt[1] gives the figures which various authors have compiled of the cases treated by medical means alone, and then states his own results. His series amounted to 57 cases; of these 28 were treated by operation and 14 died; 29 were treated by medical measures alone and 17 died. The total mortality was 55 per cent., and this, according to Holt, is about the average of all large numbers recorded. It must, however, be recollected that of this number a considerable percentage occurred in neglected and wasted infants, who, by the time they came under observation, had not much chance of life. Hutchison recorded 20 cases with two deaths, and others have given results quite as favourable when medical measures have alone been employed. Holt takes the view that physicians and surgeons do not fully appreciate the respective value of the surgical and medical measures; surgeons fail to realize how well a number of these infants do without operative interference, and physicians, on the other hand, fail to recognize how valuable may be the result of an operation performed at the right moment and with sufficient rapidity. Accordingly, he recommends that, when a child is holding his own with

medical treatment, operation should be deferred, because such a patient will generally do well and recover without any permanent damage and with no risk of recurrence. On the other hand, when a child is still vomiting and not putting on weight, the services of the surgeon should be requisitioned early.

Downes's[2] paper records the results of 22 consecutive cases in his own practice; of these, 7 died. The operation done in 21 of these children was posterior gastro-jejunostomy; in the remaining case partial pyloroplasty. Downes is so impressed with the successful results which follow on early operation in such cases, that he adopts the view that operation is indicated directly the diagnosis is made. He quotes the figures of Scudder of Boston; 17 cases with 4 deaths; and of Richter of Chicago with 23 cases and 3 deaths.

It certainly seems to the critic that Holt's position is on the whole the sounder; as he says, to operate in every case is to ignore the fact that at the lowest estimate 50 per cent. get well without operation, and so far as can be ascertained suffer no further trouble from the disease. If the physician will be readier to invite the assistance of the surgeon in those cases which are not doing well, there does not seem to be any reason why the mortality of this condition should not be reduced; but the wholesale operation on every case which is diagnosed would, we believe, tend to raise the mortality. Posterior gastro-jejunostomy, except in the hands of those who are experienced in the handling of surgical measures in young infants, must be a very dangerous procedure. It is only just to Dr. Downes to add that, in insisting on the urgency of operation so soon as diagnosis is made, he makes a point that a tumour should be felt. The writer has seen more than one case operated on without this precaution, and at the subsequent autopsy not merely no tumour, but no evidence of stenosis.

Another review dealing with the same subject is published in the *Archives of Pediatrics* for November, 1914. In this paper, Reuben[3] gives figures combined from various sources. Of 88 cases medically treated, 83 recovered; of 61 treated surgically, 47 made a good recovery. He also gives an instructive table of 185 operations, describing the nature of the

operation done and the results, from which it is evident that the most favourable operation is pyloroplasty. Of 43 pyloroplasties 29 recovered and 14 died; while of 86 gastro-enterostomies 42 recovered and 44 died. Reuben is of much the same opinion as Holt that there are cases which require operation, but that in a considerable number medical measures will suffice to establish a cure. He has used for purposes of differentiation a duodenal catheter, and believes it possible to distinguish by this means cases of mild obstruction from those obstinate and severe cases which urgently require surgical interference.

THE USE OF PROPRIETARY FOODS FOR INFANT FEEDING.

Dr. Coutts's report[4] to the Local Government Board on this subject, which is now published separately, should be carefully studied by all physicians; together with the analysis made of many of these preparations. The law on this subject is of such a character that there is practically no limitation as to what may legally be advertised as an infants' food. Thus, a food advertised as "a perfect substitute for mother's milk" was found to contain 79 per cent. of starch; and, as Dr. Coutts observes, the climax is reached when a food which contains 73 per cent. of starch is advertised as "greatly superior" to mother's milk. Another food is advertised in the following terms: "most of the so-called infants' food are mere mixtures of starchy meals and quite unfit for the delicate digestion of infants." And yet this very preparation contains 62·6 per cent. of starch. Dr. Coutts's statement is full of such examples, and should inspire every physician who reads it with a wholesome distrust of the statements so often made as to the value of the foods, which are continually thrust upon their notice.

It is an interesting speculation whether it is possible to produce in the laboratory a good substitute for mother's milk; what is certain is, that to produce such an article on a commercial scale, at a price which would not be prohibitive for all the poorer portions of the population, is quite impossible. The corollary is clear, and it is that no physician should ever countenance the use of any form of proprietary food, except as a medical measure to be strictly controlled by himself.

But though that may be sufficient as regards that proportion of the infants who come under the care of a physician, this is, after all, but a small proportion of the infants of the nation, and it is clear that legislation of a severely restrictive character is urgently required. The medical profession should make themselves acquainted with the facts as set forth in this paper, and should, without delay, head a crusade against the use of such articles as foods at all.

Dr. Coutts, in his last section, discusses the various recommendations which have been made for the adequate control of these articles, and adopts a somewhat pessimistic attitude with respect to the difficulties to be faced. These difficulties would, in fact, largely disappear if the medical profession were more familiar with the constitution of these foods and were able to describe with accuracy the constituents of any particular food. As Dr. Coutts points out, a chemical analysis attached to each food sold would not necessarily convey to the public much information, but such an analysis in the possession of the doctor would enable him to estimate the probable value of the food in question, and would render impossible the continuance of statements like those we have quoted above. Meanwhile, every doctor should make himself acquainted with the facts disclosed by Dr. Coutts, and should resolve never to sanction the use of an infants' food of which an exact analysis is not supplied. But the extermination of the evil can, we think, only be attained by a vigorous campaign on the part of the profession, of which at present we can see no sign.

THE PURITY OF COWS' MILK.

An editorial in the *Archives of Pediatrics*[5] for the month of November, 1914 is worth notice. It records that what is known as "grade B milk" was sold at 6 cents., that is threepence a quart. "Why is it possible," it proceeds, "that now a respectable bottled milk can be obtained where, and for what price, a most disreputable loose milk was once obtained?" The answer is interesting, and should strengthen the hand of those who are advocating municipal control of the milk supplies of our large towns.

New York has a Health Department wise enough to formu-

late, and strong enough to enforce, regulations which will ensure that no milk from tuberculous cattle, and no milk having more than 10,000 bacteria to the c.cm. shall be sold in the city ; that all other milk shall be Pasteurized, and that no milk containing more than 2,000,000 bacteria to the c.cm., even in the hottest summer, shall be used at all for drinking purposes. The campaign for a clean milk began with the efforts of a few medical men who had recognized the necessity for reform, and formed themselves into a Medical commission.

The story of their efforts is too long to be set forth here, but in every large city of the United States their example has been followed, and, in spite of all difficulties, the result has been that it is possible to obtain in these cities a milk at once cleaner and cheaper than is the rule in this country. It is probable that the methods adopted, and crowned with such success, would have to be modified considerably in this country, but the lesson is that it is within the power of a strong and united medical profession to bring about a reform, provided they secure the support of the municipal authorities. Such a reform cannot, however, be obtained without an active campaign on the part of the medical profession.

In connection with the question of the milk supply, two interesting papers by Delepine[6] may be noticed. He reports to the Local Government Board on the effects of certain condensing and drying processes used in the preservation of milk upon its bacterial contents. Examination was made of milks prepared by three different processes, and, though the total number of organisms was considerably reduced, Delepine found that none was sterile. The organisms which resisted the processes were chiefly sporing bacilli of the B. mesentericus type. Tubercle bacilli also survived, but apparently in a condition in which their powers for evil were considerably diminished ; at least, young rabbits fed with this milk did not contract tuberculosis, and the milk, when inoculated into guinea-pigs, produced a disease, the course of which was very much slower than that produced by the inoculation of untreated tuberculous milk.

Delepine's observations are of great value, since it has often been alleged that the introduction of the dried milk

would solve the problem of milk-borne disease.

Delepine's[7] other paper deals generally with the question of the factor of tuberculous milk in the dissemination of tuberculosis. Without entering into the question of the proportion of bovine to human infection, it is, we think, clear, from his careful summary of the methods adopted in Manchester, that the incidence of tuberculosis, especially in children, can be largely diminished by careful supervision of the milk supply. Even in Manchester, however, the proportion of tuberculous milk offered for sale is still, though much lower than in previous years, about 8 per cent. to 9 per cent., and, of course, in many other towns is much higher. As Delepine says, it is probable that when the proportion is as low as this, the danger arising from the use of the *mixed* milk is not great, but it is obvious that a still higher standard should be the aim of the medical profession.

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[2] Downes: *Ibid.*, p. 2010.
[3] Reuben: *Archiv. of Pediatrics*, November, 1914, p. 809.
[4] Coutts: *Reports to the Local Government Board*, 1914, New Series, No. 80.
[5] *Archives of Pediatrics*, November, 1914.
[6] Delepine: *Reports to the Local Government Board*, New Series, No. 97.
[7] Delepine: *Journal of State Medicine*, November–December, 1914.

SHOULD VASO-CONSTRICTORS (ADRENALIN, PITUITRIN) BE USED IN EMERGENCIES, ESPECIALLY SURGICAL SHOCK?

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During the last few years, these drugs have been strongly recommended for use on account of their "tonic effect on the circulation," not only in emergencies such as shock due to operations, but for the same reason in various acute and chronic diseases as well.

This article is intended to deal with their value, or otherwise, in the former conditions only, although some of the facts, to which attention will be drawn, have a practical bearing as regards the latter. Further, it refers to adrenalin when given by intravenous injection only, for, as remarked by Professor Noël Paton (The Practitioner, January, 1915), no general effect follows when given by the mouth, and when given intra-muscularly or subcutaneously, its rate of absorption is so variable, that it is uncertain and dangerous. This is, no doubt, true under normal or nearly normal conditions; consequently, in grave emergencies, when circulation and absorption are approaching a standstill, it is difficult to understand how effects, particularly immediate ones, can be trusted to follow the subcutaneous or even intra-muscular injection of adrenalin, pituitrin, or any drug whatever.

Adrenalin, when injected into the blood vessels, according to the above named and other authorities, stimulates the terminations of the sympathetic fibres in visceral muscle and in glands, acting on these terminations alone, and not on the muscle-fibres. One effect is to constrict arteries and arterioles, chiefly the abdominal, so that the flow of blood to the limbs may actually be increased; there is little effect on those of the lungs and brain, which become congested, and the coronary arteries are even dilated. It stimulates the corresponding nerves of the heart, causing acceleration and augment-

ation of the beat, but this action is soon masked by a reflex inhibitory action of the vagus, which, as the blood-pressure rises, causes a secondary slowing or even temporary arrest.

It seems doubtful whether under normal conditions the secretion exerts a constant tonic effect on the blood vessels; but however this may be, under abnormal conditions, such as pain, fright, irritation of peripheral nerves, an excess is quickly poured into the blood with characteristic results.

Pituitary extract causes contraction of involuntary muscle, including that of the coronary arteries, the consequent rise of arterial blood-pressure being prolonged as compared with that produced by adrenalin; the heart is slowed and its beat augmented. These effects do not follow excessive or repeated doses.

Constriction of arteries raises the blood-pressure in them and in the larger arteries, but lowers that in the capillaries, and affords an obstacle to the output of blood from the heart, which may become overdistended and unable to contract.

Coming now to the application of these observations to the treatment of emergencies, as the word "shock" has been used with various significations, I must first explain that by "surgical shock" I mean a condition brought about by excessive traumatic or operative peripheral stimulation, and that I refer particularly to that stage which is accompanied by fall of blood-pressure and loss of pulsation in accessible arteries, such as the radial.

Under abnormal conditions, the use of vaso-constrictors might be advised, on account of the supposed general function of the secretion, or of its "segmental expression."

The sudden rise in the amount of secretion, which occurs in the circumstances above-mentioned, has been regarded as a protective reaction of the organism, which should be assisted by artificial means, when the organism appears unequal to the task.

Often, however, a "protective reaction of the organism" is ill-regulated and in itself injurious. For instance, fatal laryngeal spasm may be set up by a cause comparatively trifling, and the death of a patient with unrelieved strangulated hernia is due largely to exhaustion by pain and vomiting.

If we adopt the view of Professor Sajous (THE PRACTITIONER, February, 1915), that adrenalin is an oxygen-carrier to the body in general, we may suppose that an increased supply may in that and other respects, such as increased production of glycogen, benefit muscles concerned in defence or flight, including the cardio-vascular muscles; on the other hand, the disturbance of the heart's rhythm, and the lowering of capillary blood pressure in the body-muscles are by no means favourable to self-protection. Certainly, if the pallor and helplessness, perhaps fainting or death, which are apt to follow sudden and severe agitation of mind or body can be traced to increased output of secretion from the adrenals rather than to reactions purely nervous, one will hardly be induced to administer an additional dose. One feels, indeed, inclined to speculate whether such a reaction of the organism may not be akin to that which, in some lower organisms, causes as a last resource a mimicry of death when danger threatens. Besides, when in practice we are dealing with abnormal bodily conditions, we do not encourage "natural" reactions which might possibly be of benefit to the patient in different circumstances, but in the existing circumstances are inconvenient or harmful. In filling a bladder for cystoscopic examination, one does not use an irritating fluid in order to promote expulsive efforts.

It seems by some to be considered a sufficient reason for the use of these drugs that they "raise the blood pressure," and may thus perhaps restore a lost radial pulse.

For the sake of completeness, it may be well to recall that arterial blood-pressure is raised by three factors which act in varying proportions in different cases:

1. By increased rate and power of the beat of the heart;
2. By increased contraction of arterioles;
3. By increase of the total quantity of blood in the body, and is lowered by the reverse.

Blood-pressure in the capillaries is raised: (1) by *dilatation* of the arterioles; (2) if these remain of the same calibre, by increase of arterial pressure due to (1) (3) above; and (3) by narrowing of veins, or any condition, such as effects of gravity, which increases venous pressure.

Under normal conditions, tonic contraction of the arteries

serves : (1) to maintain arterial blood-pressure, so that blood is delivered to the capillaries in a continuous, and not an intermittent, stream ; (2) to regulate the amount of blood in any given tissue. There is no reason to suppose that the muscular walls of the arteries have any peristaltic action in delivering blood to the tissues; on the contrary, their constriction obstructs its progress to them. If the former were true, increased action in such cases as we are considering would be detrimental, for what is urgently needed is not a relatively better supply to the limbs and abdominal viscera but to the heart and medulla, and the coronary and intercranial arteries do not share in the constriction. It may be remembered that ergot was a routine remedy for hæmoptysis, until it was pointed out that as a vaso-constrictor it did not affect the pulmonary arteries, and so actually diverted blood to the lungs from the general circulation.

Here, especially when the total amount of blood in the body has been reduced, we *want* to get a diversion to vital centres, and so far as this goes the effect of a vaso-constrictor is beneficial. In shock, however, especially when accompanied by hæmorrhage, low arterial blood-pressure is not due only to laxity of vessel walls but to lack of output from the heart as well, and the radial pulse should be regarded chiefly as an indication of the working of the heart and not as being in itself important.

Far more important is the possible effect of artificial constriction of arteries upon a heart already over-taxed, but this seems to have received comparatively scanty consideration.

Under ordinary conditions, the chief "peripheral resistance" to output of blood from the heart is in the medium and small arteries, and not in the capillaries; the total area of the latter is so great that the system may be compared to a lake with narrow inlets.

By tightening up arteries, a tired heart is further embarrassed. Although the stimulation of its augmentory and acceleratory nerves causes it at first to strive to overcome the difficulty, there is the danger already mentioned, that it will fail to do so, become over-distended, and give out altogether. It is hardly necessary to add that the human heart is often, or nearly always, more liable to this

disaster than that of an animal. Hence, we must not trust too much to experiments made in the laboratory.

I believe the ill-effects attributed to adrenalin used during light chloroform anæsthesia, in cases recorded by Dr. Levy and others, may be explained by the fact that it was *injected submucously* and probably entered a vein, so that general effects at once followed as above described, the heart being already affected by the chloroform. It must not be forgotten that stimulation of the nasal nerves, indeed those of any orifice, especially under too light anæsthesia, has a marked and similar effect on the circulation, so that in such cases is present the resultant of two forces acting in the same direction. I have never known any harm done by its application to a bleeding surface, its action being then only local.

In cases of shock, when there has been no great loss of blood, I would, therefore, rather advise the use of vaso-dilators such as ether (open), nitrite of amyl, and brandy, with the customary application of hot-water bottles, etc. One object, amongst others, is to lessen the resistance to the contractions of the heart, and the "natural protective reaction" is, indeed, counteracted rather than assisted in this respect. To these may be added artificial respiration, with oxygen, and massage of the heart when occasion requires.

When there has been much loss of blood, with or without shock, it is conceivable that vaso-constrictors by filling up the heart and diverting blood to coronary and intracranial systems may be beneficial, but their action is so difficult to regulate, and the condition so critical and complicated, that even then their use seems to me hazardous. If there is shock, it may be that too much adrenalin has already been secreted. Saline infusion, raising of the limbs, lowering of the head, and, when possible, pressure on the abdomen, are well tried and hopeful methods, to which, as far as I know, no objection can be made. I believe that any benefit, which has followed injection of a vaso-constrictor in saline solution, should be credited to the vehicle and not to the drug.

It need hardly be added that in either event, further injurious impressions should, as far as possible, be avoided, or reduced by the use of anæsthetics, analgesics, or narcotics as may be indicated.

TUBERCULOSIS IN INDIA.

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It is my privilege to call attention in this paper to the general prevalence of tuberculosis in India, to the causes underlying the spread of the disease, and to the remedies that are likely to help in its cure and prevention. Introductions from the India Office to some of the Governors in India enabled me to visit many parts of the country after an absence of 20 years, and to investigate on the spot some of the problems connected with tuberculosis. My tour extended from Bombay to Rangoon in one direction, and from Nepal and Calcutta to Madras in another. I have returned with the conviction that tuberculosis has made a considerable advance during the last 20 years.

Sir Leonard Rogers estimates that 25 per cent. of the bodies examined post-mortem in Calcutta Medical Hospital showed signs of latent or active tuberculosis.[1] The disease seems more common at present in India than in England. It is one of the common and fatal diseases in Calcutta. In fact, the mortality in Indian cities like Bombay and Calcutta is considerably higher than in Glasgow, Birmingham, and Manchester.[2] The annual reports of the Surgeon-General, Madras, show a steady increase year after year in the returns of tuberculosis since 1901. Taking from 1901 to 1905, the number of cases treated increased by 50 per cent., and from 1901 to 1910 by 100 per cent. The death-rate from tuberculosis in the Madras General Hospital has doubled in 1913, as compared with 1912. It is more prevalent in densely-crowded cities than in villages. Rogers considers that it is more common among the female than among the male population, owing to insufficiency of air and bad ventilation in the zenanas, and therefore more common among the Mohamedan than the Hindu females. Owing to damp, poverty, and insanitary conditions, the disease prevails more among the dwellers in

huts than those who live in brick buildings. All parts of India: Bombay, steamy, but with more even temperature; Punjab, where variation is most marked; Calcutta and Lower Bengal, low-lying and with moist heat; Central Provinces, Madras, with great heat; high elevations like Cashmere, Nepal, Nilgiris; Burmah, Malabar, with big rainfall; all tell the same tale of widespread distribution of the disease throughout India.

We have no reliable statistics as to the extent of mortality from tuberculosis from the whole of India. Many a case is either missed or mistaken for malaria, enteric or other continuous fevers, bronchitis, broncho-pneumonia, etc. More than half the total number of deaths in India (four out of seven million deaths) are attributed in the returns to "fevers." The classification in the registration of deaths being vague and misleading, large loopholes occur whereby many cases of tuberculosis are certified under "respiratory diseases other than phthisis, pyrexia of unknown origin, other fevers than smallpox, etc.," so that there is every reason to believe that the number of certified deaths is far below the actual number.

There is, however, one source of information which gives, more or less, an accurate idea of the extent of the ravages of consumption. It is contained in the report of the Oriental Insurance Company, which has its policy holders in all parts of India. From the reports of the number of deaths among the Company's policy holders, we gather that tuberculosis claimed a mortality of 9 per cent. in 1911, which steadily rose to 10½ per cent. in 1912, and 11½ per cent. (11·6 to be more accurate) in 1913;[3] which means that the rate of mortality among the insured was about 1 in 11 in 1911, 1 in 9 in 1912, and 1 in 8 in 1913.

If we base our calculation of tuberculosis mortality for the whole of India on these figures, it would not be an exaggerated estimate, for the insured were more or less picked healthy lives when they commenced with the Insurance Company, and the rate of mortality for all classes and conditions of Indian people must, therefore, be considerably higher. Taking the population from the census returns for 1911 as 244,267,000 for British India, and 315,000,000 for

the whole of India, we arrive at the conclusion that, roughly speaking, tuberculosis claims an annual death-rate of 906,719 in British India, and 1,169,280 in the whole of India. Looking at the figures in another way, the equivalent of the whole of the population of Calcutta is wiped out in a year from its ravages. If malaria is responsible for more than a million deaths yearly, tuberculosis will soon outstrip malaria in annual mortality, if it has not already done so.

It is very interesting to study the causes that have brought about such a wide and increasing prevalence of the disease in India, for they throw a great deal of light on some of its problems in other countries. I want to approach this question, not only from a humane, but from a scientific point of view, without any previous bias or prejudice. Tuberculosis follows the wake of every civilization, ancient and modern, which has produced social and economic changes for which man was ill prepared. It is this failure to meet new conditions, to adapt himself to new environment, that has produced a group of changes in its constitution which has ultimately developed into tuberculosis. Let us look at one or two pictures of India, past and present, and see if they can help us to understand the causes underlying its morbidity in that country.

Sir Thomas Munro, writing not a century ago, said that "if a good system of agriculture, unrivalled manufacturing skill, a capacity to produce whatever can contribute to either convenience or luxury, schools established in every village for teaching reading, writing, and arithmetic, the general practice of hospitality and charity amongst each other, and above all, a treatment of the female sex full of confidence, respect and delicacy are among the signs which denote a civilized people—then the Hindus are not inferior to the nations of Europe."

Lord Minto, grandfather of the late Viceroy, speaking of the Bengalis wrote the following in 1807 :—"I never saw so handsome a race. They are tall, muscular, athletic figures, perfectly shaped and with the finest possible cast of countenance and features. Their features are of the most classical European models with great variety at the same time."

An eminent Indian gentleman (Mr. Moti Lal Ghose) speaking in the All-India Sanitary Conference in 1912 said :—

"I was born and brought up in a village in the interior of Jessore which was generally known as a fever-stricken district. Yet 60 years ago there was very little disease in it, and this was the case with most of the villages in Bengal. We had at that time plenty of mosquitoes but no malarial fever. Cholera was practically unknown. So were phthisis and other respiratory diseases except asthma. . . .

Five or six decades ago there were few towns or municipalities in Bengal. The pick of the nation lived in rural areas. The result was that the bulk of the villages were furnished with all the necessaries of life. They had an excellent system of drainage, and each of them possessed at least half a dozen tanks, one or more of which were reserved for drinking water. They rubbed their bodies with mustard oil, and bathed at least once during the day. They lived in well-ventilated houses facing south, as a rule, and having large compounds. Fields were set apart far from human habitation for latrine purposes. They had abundance of food. There were scarcely a family, however poor, who had not one or more milch cows. Rivers abounded in fish, and rice and other cereals were very cheap. Villages in those days teemed with healthy, happy, and robust people who spent their days in manly sports—in wrestling, and playing lathis and swords, in swimming, riding and running, and not troubled by the bread question or the fear of being visited by any deadly pestilence; had wholesome food and drinking water, kept their villages dry by natural drainage; had not to struggle hard for their bread; had enough of grazing lands for their cattle and such nourishing food as milk and fish."

He then proceeds to give a picture of Bengal of to-day:—"The people are dying like flies from malaria. The Bengali race is dying and must ultimately disappear like the Greeks of old, who also fell a prey to this disease, unless vigorous steps of the right sort are promptly taken to save them from extermination . . . . There is no longer a sufficiency of food and good drinking water to enable the villagers to nourish their bodies. Food is scarce and healthy food absolutely rare. Where are our cattle? Almost all gone. The milk is bad in quality. The water which millions drink is veritable poison. Almost every village is full of

noxious jungle and weeds and saturated with subsoil dampness, and no fields which serve the purpose of latrines."

What do these pictures signify? They mean that in the tremendous impact between the ideals of the east and the west, the east has more or less succumbed—the east with its primitive and pastoral habits, its open-air life in the villages, its tank water-supply, its field latrines, its free grazing lands, its simple handicrafts and industries, its spiritual outlook and quiet peace, clashing with the west with its extensive organization, its great commercial development, its machine-made goods, and its industries, its bustle and clamour of interests, its material outlook, its strenuous life and struggle for existence. Europe's phenomenal progress in commerce and industry took the Indian ryots, the weavers and the artisans, by surprise, and brought about a state of things for which they were not prepared.

What was the result? The crushing of the indigenous industries, the unemployment, the migration from the villages in search of employment, and consequent overcrowding of towns with high rents and dear food brought conditions of want and poverty. Malaria followed the neglect of the villages and their sanitation; and the constitutions, enfeebled and prostrated by poverty and malaria, easily fell victims to plague, pestilence and famine. To complete the picture, the adoption of European standards of living and the increased facilities for drink and enormous consumption of alcohol, which is yearly growing, have intensified the effects of misery and poverty and prepared a soil for tuberculosis. Thus India presents a condition similar to that of England 30 or 40 years ago—a cycle of evils beginning with neglected country, crowded towns, insanitation, underfeeding, slums, strenuous life, and ending with drink, degeneration, and disease.

Owing to the rapid growth of towns and cities, the absence of free grazing lands and increased expense of feeding cattle, the very common articles of diet like milk, butter, and ghee have not only rapidly advanced in prices but cannot be had pure or of good quality. Dr. Srinivasa Rau, Director of Public Health Institute, Bangalore, reports that pure and unadulterated milk is not available for 90 per cent. of the people living in large towns, and because of this difficulty many of the poor

and even middle-classes resort to the use of condensed milk and various patent foods. Another article of food widely used is ghee—butter clarified by heat. The price of ghee has gone up beyond all reasonable bounds, and it is shockingly adulterated with various animal fats and vegetable oils; even the adulterated article fetches now a higher price than what the pure ghee did 20 years ago. When we consider that the prevailing rates of wages for millions of unskilled labour are not more than from two to three pence a day, we can see that any increase in the prices of the bare necessaries of life soon overreaches the margin of subsistence and must result in underfeeding or starvation. The import of large quantities of condensed milk, tinned butter, and other artificial foods in place of fresh dairy produce, also accounts for a large infantile mortality and the defective nutrition of the poor.

In India, consumption very often goes hand in hand with malaria. The tropical heat and dust aggravate the symptoms, and help the disease to take a rapid course. The social customs of the people such as early marriage, intermarriage with near relations, expectoration, etc., are, no doubt, factors that predispose the soil, though there is a tendency to exaggerate their evil effects. I was pleased to find any number of cases of healed tuberculosis in places like Nepal, where, though the sanitation is primitive, life is not strenuous, thus confirming my experience in England that want and anxiety more than insanitation renders the organism susceptible to this disease.

But we must go behind poverty, malaria, overcrowding, and low wages, behind even the social habits of the people, to trace the source. Behind all these physical causes stand mental stress and anxiety. The ceaseless advance of western civilization has brought in its train a great unrest among the Indian people—social, mental, moral, and spiritual unrest. The slow, easy-moving east has been caught up by the rush of the onward tides of western thought, and this surging sea of unrest has profoundly disturbed the calm and peace of centuries; ancient faiths have lost their anchor, and this drifting into the unknown sea, this mental stress and strain have intensified the physical causes of inefficiency,

and increased the impairment of healthy metabolism and nutrition.

What, then, is the connection between civilization and tuberculosis in India? Civilization has brought about certain changes in the life and habits of the people: in the villages, the decay of home industries by foreign competition, migration into towns, neglect of village life, overgrowth of jungle, defective sanitation and drainage, impure water supply, malaria, physical deterioration; in the towns, overcrowding, competition, high rents and dear food, the consumption of adulterated and artificial foods, cramped space and foul air, slums, insufficiency of food, intemperance, physical degeneration.

These conditions of wrong living — factors in common with other countries—coupled with the social customs of the people, and aggravated by anxiety and mental strain, and continued for one or two generations, have brought about changes in the two vital functions of the organism, viz., nutrition and respiration. They have hindered the normal processes of digestion and assimilation, poisoned the cells of the blood and tissues, lowered resistance, and produced degeneration and disease. Moreover, the series of changes that have taken place in India, during the last hundred years, offer a striking illustration to my contention that tuberculosis is caused not so much by an enemy from without as an enemy from within; *i.e.* man's wrong living under civilized life has created constitutional changes in the blood and tissues, which have culminated in disease. Take this fact. The Indian population, which suffers from poverty, hardship, scanty clothing, and insufficient food, succumbs to fever and tuberculosis in a much larger proportion than the Indian troops, who are better fed, clothed, and housed, and are under better sanitary conditions.

After a close study of tuberculosis for nearly 20 years, I am convinced that it is not so much an infectious disease as that it is due to a chronic disorder of nutrition, a dyscrasia, a degeneration. Whether this defective nutrition and all its consequences are the failure of the effort of nature to meet new conditions, or the effort itself—in other words whether it is physiological or pathological—this is not the time or the place to discuss. If there be infection, man has created

conditions of infection by his own folly and sins against physical and moral hygiene.

The tendency of the present day is to exaggerate the importance of tubercle bacillus in the causation of tuberculosis. I still maintain that tubercle bacillus is a saprophyte found in water and in grass, in milk and butter, and that man's changed environment and habits of civilization have given it opportunities to alter its saprophytic nature, and assume more or less pathogenicity.

Even the theory of milk infection must be considerably modified by the light thrown upon the question by countries like India. There is practically very little tuberculosis among Indian cattle. Millions of Indians do not drink cow's milk, owing to its dearness or the difficulty of obtaining it pure, but largely use condensed milk instead, and still, as we have seen, consumption is very prevalent among them. So, in Japan, where, Kitsato says, the native cattle are unknown to suffer from tuberculosis. The consumption of milk is particularly small, and he works it out to be $2\frac{3}{4}$ teaspoonfuls per day per head, and cow's milk in feeding children is practically unknown ; yet, tuberculosis is prevalent. So in other countries like China, Siam, Egypt, Persia, Asiatic Turkey, Roumania, Gold Coast, etc., where little or no milk is consumed, tuberculosis is rife. In England, it is more common among the poor who drink very little milk as compared with the well-to-do classes.

The truth is that it is not the consumption of milk, but the want of good, pure milk in its raw, fresh state, and the substitution of artificial foods which creates in children a disorder, a diathesis, a degeneration which sooner or later culminates in tuberculosis. We have been so prepossessed with the theory of milk infection, that we have not considered if tuberculosis may not be the expression of physiological or pathological changes, caused by poor nutrition and impaired metabolism, where the organism is unable to maintain a normal blood reaction and a healthy adjustment between cells and tissues. Whatever be the causes (and the problem is not solved yet) certain it is that tuberculosis is the expression of man's hunger, of food hunger, air hunger, land hunger and rest hunger, caused by unhealthy living and vicious conditions of modern civilization. It is only by studying

all the social, economic, and clinical factors in a broad, comprehensive spirit, that we can ever hope to come near the right solution of tuberculosis, and find a satisfactory remedy for any country.

What are the remedial measures that are likely to stay the ravages of this black plague in India? India is a large country, and any attempt to draw up a scheme for three hundred millions of people of many castes, tribes, and conditions would be a gigantic task. Here, we can only touch some of the main principles that will help us in the treatment and prevention of the disease.

GENERAL.

1. *Country.*—The open-air treatment has been so successful in this country ever since its inception some 15 or 16 years ago, that it can well form a basis on which to deal with the disease in India. The open-air movement taught us that improved social conditions, the cheapening of food, the application of fresh air and sunlight in dwellings, factories, etc., the improvement in sanitation, water supply, etc., are agencies that make for the efficiency of a people. Sir Hugh Beevor has pointed out "a coincidence, and a remarkable agreement between the fall in the phthisis rate, the fall in the price of corn, and the fall in the number of paupers and the rise in the money wage."

There is not the slightest doubt that the increased well-being of the people in this country, obtained by the cheapening of the necessaries of life, has done more to diminish the death-rate from consumption than any other factor, such as sanitation, the discovery of the bacillus, or notification. So it will be in India. Tuberculosis is chiefly a poverty disease among the poor in India as in England, and any cheapening of food and improvement in the rate of wages or fixed incomes will reduce poverty, and raise the resisting powers of the poor against tuberculosis. Above all, the open-air movement has brought home the lesson that by multiplying towns with their bustle, noise, and strenuous life we have multiplied disease, and that country life alone will bring salvation and health to the people.

For nearly a century England has suffered from the horrors of factory and industrial life, and has naturally raised the cry,

"back to the land." And if India is to take a lesson from the mistakes and miseries of Europe, she will, before it is too late, return to nature and find her health and peace in the fresh air and the open country. Therefore, the first duty of the Government and the social reformers in India should be to make every effort to keep the people in the country by making it attractive and habitable and by reviving village life. This can be done :

(*a*) By attention to rural sanitation, hygiene, the clearing of jungle, the provision of pure water supply by digging of wells, the organization of conservancy. The granting of free grazing land would revive the dairy industry, cheapen dairy produce which is the staple food of the people, and reduce infant mortality.

(*b*) By reviving agricultural industries. India is pre-eminently an agricultural country, more than two-thirds of the population being rural and dependent upon the land. The condition of the farmer, the raiyats, who are miserably poor, should be improved by giving them a more permanent interest in the land, by co-operative credit societies which would free them from the cruel hands of the money lender, by agricultural training which would enable them to improve their crops. The Indian gentlemen and landed aristocracy would give a great impetus to agriculture if they would take to scientific farming, and teach the raiyats better and more profitable methods of cultivation.

(*c*) By promoting indigenous arts and industries in the country such as weaving, etc., so that the artizans will find work in the village, and thus reduce congestion of the towns. Therefore, I earnestly hope that the Government of India and the Indian reformers will give their first attention to the claims of the country, remembering that the health and the prosperity of India depend upon the development of country life.

II. *Towns and Cities.*—The claims of the cities, which although only amount to 8 to 10 per cent. of the population, cannot be ignored, and embrace improved sanitation, drainage, pure water supply, town planning with a view to wider thoroughfares, sufficient air, light and ventilation, roads through congested areas, the provision of open air spaces in the shape of parks and gardens, cheap lodgings for the poor that can be

let at a low rental by the municipality, distribution of the population to the suburbs by cheap train service, hygiene taught in the schools, the inspection of pure milk supply—all these sanitary measures will promote the efficiency of the people and help to solve the tuberculosis problem in the towns.

SPECIAL.

Medicinal Remedies.—Two kinds of medicinal remedies claim attention in the treatment of consumption—tuberculin and continuous inhalation. Medical opinion is still divided as to the of efficacy tuberculin in the cure of pulmonary tuberculosis, and any establishment of tuberculin dispensaries in India is at present both unwise and uncalled for. In my recent tour, I was rather surprised to find tuberculin recklessly and indiscriminately used by medical practitioners, and even by unqualified men in India. India in this respect, as in other concerns like milk and patent foods, is overrun by the commercial enterprise of unscrupulous men who are exploiting that country to their own advantage. My experience of tuberculin goes as far back as 1906, and, on the whole, I am not in favour of its general use. On the other hand, I have been using continuous inhalation in connection with the open-air treatment for the last 15 years with excellent results.

Any panic legislation will do more harm than good. It was rightly pointed out at the Lucknow Sanitary Conference in 1914 that any legislative proposals to improve the quality of the milk, or licensing, would still further increase the price of milk, and make it altogether prohibitive for poor people. It is not so much by legislation, but by patient education of the people, not by restrictive laws as by co-operative measures that we can help the Indian people to fight against the ravages of consumption. Therefore, I am not greatly in favour of compulsory notification or segregation of consumptives in India. For it would cause, even more than it has done in England, an undue scare, fright, phthisiphobia, and unnecessary suffering of the consumptives, who would be treated as pariahs and lepers. Besides, as Dr. Lankester pointed out at the Lucknow Conference, it would lead to the oppression of the people and increased opportunities for peculation by petty officials, and perhaps

increased political ferment and unrest. Moreover, in the broad light of clinical observation of to-day, we have reason to doubt tuberculosis being strictly an infectious or contagious disease.

Dispensaries, Special Wards and Sanatoria.—Now coming closely to the practical problem how to grapple with consumption as it exists to-day, I am in favour of the dispensary system in India to serve as a central bureau and sorting house which would work in connection with the hospitals and sanatoria. The general hospitals should have special wards set apart for tuberculous cases with open-air galleries, where a modified form of open-air treatment could be carried out. Early cases could be treated in sanatoria erected on suitable sites, at an elevation of 4,000 to 5,000 feet, to ensure a cool atmosphere and equable climate, like Bharwali, Almora, in the north, and Kodaikanal on the Palnis in the south.

But the difficulties of caste system and the conservative customs and habits of the people would stand in the way of a general adoption of the sanatorium system in India, as it exists in England or Europe. The Indians, as a rule, are not inclined to leave home and their relations to seek treatment in a sanatorium, especially if it is far away. Therefore, I am strongly in favour of a system of village colonies, carried on somewhat on the lines of garden cities in this country, where consumptive patients could go and live with their families and at the same time carry out the open-air treatment under ideal conditions. These village colonies would be model villages situated not far from big cities or towns, and embrace all the agencies for the cure and prevention of the disease. They would contain groups of cottages or houses with large gardens, erected on hygienic lines with provision for plenty of air and light and ventilation. Wide avenues and parks and artistic buildings would adorn the colony and give it the appearance of a garden village. The village would also contain a hospital, a sanatorium, a school for children, who would be taught in the open air ; a farm, a dairy, a laundry, temples or places of worship, a public hall, which could be utilized for lectures on hygiene and other subjects of interest.

Patients in the early stage of the disease could be treated at home or in the sanatorium, and, if very ill,

could be removed to the hospital. Suitable patients and other residents, if they wished, would receive technical training, training in agriculture, gardening, dairy industry, carpentering, weaving, book-keeping, etc., and the work done would be part of their treatment in graduated exercise; at the same time, it would provide an occupation for the future, and thus would solve the after-care problem. The colony would attract those weak in health or predisposed to tuberculosis, and professional men in search of health. Their children would be taught in the open-air schools. Thus the colony would embrace many activities, and become a centre of education and training for miles round.

I am sure some such scheme, earnestly carried out by the various municipalities with the aid of the Government, would go a long way to solve, not only the problems of tuberculosis, but other social and economic questions. It need not be expensive to carry out such an organization. The colony could be made partly self-supporting and partly helped by the municipality or the Government. Private philanthropy could step in, too, and give a practical turn to the scheme by financing a colony here and there. Here is an opportunity for Indian reformers and princes to show their sympathy with the people by their munificence and volunteer work. The health and salvation of India mainly depends upon the people themselves. Therefore, above all, India wants a new impetus, a new enthusiasm, a new life that shall give a stability of character, a sympathy and solicitude with the suffering of the people, a strength for sustained effort to carry out the necessary reforms. The Government of India on their part will require great patience, forbearance, and great sympathy to lead in the path of reform and efficiency. Thus, by mutual co-operation and goodwill, tuberculosis need not be the menace in the near future that it is at the present day.

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RECENT WORK ON DENTAL SURGERY.

By J. G. TURNER, F.R.C.S., L.D.S., R.C.S.

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In the course of an article on "The Possibilities of Research into the Etiology of Anomalies of the Jaws and of Malocclusion," Julius Zundler[1] (Vienna) asserts that by means of a stereogrammatical method, using X-rays, he can "reconstruct plastically, within a fraction of a millimetre, the bones of living beings." He promises to use the method to ascertain the reality or falsity of the claim made by some to widen the floor of the nose and straighten the vomerine septum by expansion of the dental arch, and hopes eventually to publish results.

HALLUCINATIONS AFTER COCAINE.

V. E. Henderson[2] quotes numerous cases of erotic hallucinations following the use of cocaine as a local anæsthetic, and warns dental practitioners against its use, unless a third person be present. A case is quoted in which cocaine pressure anæsthesia was used to deal with an exposed tooth-pulp. Later the patient, a girl of 16, made charges of indecent assault against the dentist.

SALIVA AND DENTAL CARIES.

Bunting,[3] in an article on "The Saliva and Dental Caries," discussing the rôle of mucin, says: "From this we may infer that the solids of the saliva, mucin, glycogen, and other substances, have carbohydrate food to furnish a certain amount of acid, and, if continually replenished, might be sufficient to carry on the process of caries; but as compared with the ingested foods, which remain in the mouth for some considerable time, the salivary solids are inferior in their ability to produce acids."

RUMINATION.

R. Klein[4] details a case of rumination in a man. The

man swallowed his food in large pieces, and about half-an-hour later lay on a sofa and comminuted his now softened food at leisure and with no feeling of disgust. The habit seemed to have arisen at school, when defective teeth obliged him to bolt his food in order to keep pace with his fellows.

FACIAL RESTORATION.

L. Caillou[5] describes a method of facial restoration by means of a preparation of formalized gelatine, thickened with kaolin. The false part is coloured and fixed in place by means of a varnish cement. The formulæ are given.

CHRONIC SUPPURATION—ANTRUM.

R. Moreaux[6] advocates the treatment of chronic suppuration of the maxillary antrum by means of the vapour of heated iodoform, introduced through a tube passed up the socket of an extracted tooth.

TUBERCULOSIS AND DENTAL CYSTS.

Victor Frey,[7] quoted from the *Oesterr. Zeitschrift für Stomatologie*, thinks it possible that there is a relationship between tuberculosis and dental cysts. Zilz, he says, has demonstrated, in an irrefutable manner, the virus of tuberculosis in the cyst contents.

RECURRENT DISLOCATION OF JAW.

M. Nauenburg,[8] quoted from the *Deutsche Zahnartzliche Zeitung*, describes two forms of apparatus which he has used with success in the treatment of recurrent dislocation of the lower jaw. The apparatus is fixed to the teeth and worn with little inconvenience.

EFFECT OF NOT WEARING DENTURES.

"Fiat Experimentum"[9] relates his personal experiences of the edentulous state during a period of 10 weeks, having previously for some years used full upper and lower dentures. He experienced practically no difficulty with the everyday food of civilized life, had no gastric troubles, and maintained his normal weight. His sense of taste was distinctly im-

proved.

PYORRHŒA ALVEOLARIS.

H. N. Znamensky [10] argues that pyorrhœa alveolaris begins as an osteoporosis of the bone, and that this is a sequence of arterio-sclerosis. He considers the disease constitutional.

IMPURITIES IN "GAS."

W. B. Hart and F. W. Minshall,[11] as the result of an inquiry into the impurities in commercial N_2O for dental use, conclude that nitric oxide is the impurity that calls for special attention. Only the purest raw material should be used, and the gas passed slowly through a large volume of purifying liquid.

SOFT WATER AND CARIES.

J. B. Cook [12] finds a correlation between the softness of water and the incidence (excess) of dental caries. Urban areas only were considered, but he thinks environment can be ruled out. He notes that this correlation may not be one of cause and effect.

RESTORATION OF DEFORMITIES.

Martinier and Lemerle [13] have published a useful handbook on restoration of deformities of the face following injury, etc. which is well worth the attention of military surgeons.

JAWS AND TEETH IN ANIMALS.

J. F. Colyer [14] publishes an instructive series of illustrations of pathological conditions of the jaws and teeth in animals. The original was a museum demonstration given at the Royal College of Surgeons.

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CASE WITH COMMENTS.

AN INTERESTING CASE OF MASTOIDITIS.

By L. C. V. HARDWICKE, M.B.

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DR. WILLIAM WILSON, of Manchester, has recently recorded two unusual cases of mastoiditis in children.[1] The following case, that of an adult, is similar in many respects to the first of Dr. Wilson's cases, and is too, I think, of considerable interest.

W. W., a Cornishman, aged 35, a skilled mechanic in charge of the mill (crushing tin ore), came to me on the morning of November 18th, complaining of a dull pain with occasional sharp twinges localized to the right mastoid; although he had not been feeling well during the previous three or four days, he had experienced no pain until the early hours of that morning. A little swelling and redness of the skin over the right mastoid were seen, and tenderness was elicited on slight pressure, and by tapping around. There was very little general disturbance, the temperature was 99°·2, and the pulse about 80. There was no pain in the ear and no deafness, and the tympanic membrane appeared perfectly healthy. The breath was foul, and the teeth were very bad, most of them had decayed down to below the level of the gums, which were unduly red and swollen in several places, but pus could not be made to exude on pressure. The tonsils, uvula, soft palate, and pharynx showed considerable congestion, and, in addition, the tonsils were somewhat swollen. He was habitually inclined to costiveness.

As an immediate operation did not seem to be called for, it was deemed advisable to treat the mouth and throat, and attend as well to the general condition. The patient was therefore given some ichthyol ointment to apply over the mastoid, an antiseptic mouth-wash and gargle, and an iron tonic with Epsom salts.

The patient showed some improvement on the second, third, and fourth days, and felt only occasional twinges of pain in the mastoid; his temperature and pulse became normal, and he said he felt "very fit." However, on the morning of the fifth day (November 22nd), he complained of having been wakened during the previous night by a sharp pain behind his right ear, radiating especially down that side of his neck. On examination, there was found increased swelling and tenderness over the right mastoid, and fluctuation was now evident. To avoid the grave risks that might result from delay, it was decided to operate immediately. The temperature had risen to 100°, and the pulse was 86. The mouth-wash had been

[1] *B. M. J.*, August 29, 1914, p. 398.

energetically used, the catarrh having practically disappeared, and the gums were distinctly better.

Schwartze's operation was performed on November 22nd. The incision was made through the periosteum on to the bone, a subperiosteal abscess being thus opened, and a fistula through the bony external wall of the mastoid process leading to the antrum became evident. A considerable amount of pus in the mastoid cells and the antrum was evacuated, and a comparatively large amount of necrosed bone was gouged away. After syringing with warm boracic lotion, a drainage tube was fixed in position, and the upper part of the wound was closed by sutures. As there was little purulent discharge afterwards, the drainage tube was removed on the second day, and the opening allowed to close. Healing took place rapidly.

The septic condition of the mouth, fauces, and pharynx would indicate that infection had travelled from them to the mastoid cells; yet there was, as in Dr. Wilson's case, complete absence of any signs or symptoms of middle ear trouble both before and after the operation. It is interesting to note how a serious condition can exist without much disturbance, for the constitutional and local signs were slight when the patient was first seen on November 18th, and, judging from the amount of softened bone found at the operation, necrosis had probably commenced about a week previously.

Practical Notes.

TREATMENT OF ECZEMA IN THE QUIESCENT STAGE.

Gougerot advises that, when the inflammatory stage has passed off, but the eczema does not tend to heal, active treatment should be applied gradually and carefully, and adapted to each individual case.

1. When the lesions are oozing, or remain fissured and moist in the folds of the skin, they should be bathed every three or five days with a 1 in 10 solution of silver nitrate, 1 in 250 aqueous solution of methylene blue, or with a 1 per cent. solution of picric acid. Afterwards, some oxide of zinc paste, pure or with tar, or tar alone, is applied and well powdered over with talc.

2. When the patches begin to desquamate, they are often still moist, and remain particularly irritable. The active bodies used must be incorporated with zinc ointment in gradually increasing proportions, from 5 to 20, or even 40 per cent. Those recommended are tar, ichthyol, tumenol, thiol, and particularly oil of cade. Gaucher uses the following :—

℞	Olei Cadini - - - - - -	ʒj.–ij.
	Zinci Oxidi	
	Talci - - - - - ana	ʒiv.
	Olei Amygdalæ dulcis - - - -	ʒij.–iij.

Misce. Fiat pasta.

If pruritus is present, camphor (ʒj) should be added.

3. When the patches are scaly, dry, and do not seem irritable, the above pastes should be used with the cautious and progressive addition of from 1 to 5 per cent. of sulphur, 1 to 5 per cent. of salicylic acid, 1 to 5 per cent. of calomel, 1 to 3 per cent. of yellow oxide of mercury, 1 to 3 per cent. of tannic acid, or 1 to 2 per cent of naphthol.

One of the happiest of these combinations is Gaucher's:—

℞	Sulphuris præcipitati	
	Camphoræ	
	Acidi Salicylici - - - - ana	gr. xv.
	Olei Cadini	
	Olei Amygdalæ dulcis - - - ana	ʒijss.
	Talci	
	Zinci Oxidi - - - - - ana	ʒv.

Misce. Fiat pasta.

Preparations which require heat for mixing are of excellent service, because the constituents then form actual combinations, and are consequently less irritating.

These pastes should only be applied at night; during the day, the parts should be covered with a plaster (zinc oxide or oil of cade).

4. When the patches remain obstinate, more active treatment must be

tried with pastes of salicylic acid, resorcin, oil of cade in increased proportion, or with yellow oxide of mercury ointment—1 in 30. If no irritation is present, the exfoliative method, used in obstinate acne, by means of *savon noir* may be used.

Gougerot's preference is for coal-tar, applied neat or in one of the following preparations:—

℞ Liquoris Picis Carbonis - - - - 3 ss.-ijss.
Zinci Oxidi
Talci - - - - - ana 3 v.
Olei Amygdalæ dulcis - - - - 3 iv.

Misce. Fiat pasta.

Or,

℞ Liquoris Picis Carbonis - - - - 3 j.
Aquæ Calcis - - - - - 3 ij.
Adipis Lanæ - - - - - 3 iii.
Paraffini mollis - - - - - 3 iv.

Misce. Fiat unguentum.

(*Journ. de Méd. et de Chir. prat.* November 10, 1914.)

TREATMENT OF PNEUMONIA.

Lévy Du Pan points out that the end and object of treatment in pneumonia should be to combat the destructive effect of the invading organism by weakening the virus of the infectious agent. General treatment directed to supporting the heart is a first necessity, for, as Bard frequently insisted, "the disease is in the lung, but the danger lies in the heart." For specific treatment, something more is necessary; anti-pneumococcus serum has been tried, but the results have not been definitely good. Anti-diphtheritic serum has been recommended, but has not been found successful. Collargol at first seemed to be the remedy sought for, but its effect by inunction is not marked, whilst subcutaneous and intra-muscular injections are much too painful. The results of intra-venous injections are about the same in pneumonia as in other infectious diseases; the temperature is brought down quickly, and the general condition is notably improved. The technique of intra-venous injections is somewhat difficult, however, and for nearly five years Lévy Du Pan has used electrargol in hypodermic injections with excellent results. A crisis is obtained at latest in 48 hours, no matter at what stage of the disease the injection is given. One injection of 5 c.c. is enough, as a rule; two have very seldom been required. He publishes six cases as typical of nearly 100 treated with no deaths. One of these cases is that of a child, 5 years old, with double broncho-pneumonia. Three injections of 5 c.c. of electrargol were given, and a good recovery was obtained.—(*Revue méd. de la Suisse romande*, January 20, 1915.)

QUINIODOL—A SUBSTITUTE FOR IODOFORM.

Mouchet and Malbec have found that, in the treatment of infected, especially of gangrenous, wounds, iodoform has proved of very great service. The fœtor disappears, and the foul scab covering the surface gives place to healthy granulations. The extremely disagreeable smell of iodoform is an objection to its use, and an efficient substitute has

been sought for and found in quiniodol, which has the advantage, due to powdered cinchona, of a pleasant aroma, and is just as powerfully antiseptic and equally keratoplastic as iodoform if not more so. The iodine is in as good a state of dilution as in the liquid form. Quiniodol has the further considerable advantage, not to be overlooked in the present time, of being very much cheaper than iodoform. The latter costs at least 60 francs per kilo., whereas quiniodol is at most from 9 to 13 francs the kilo.

The method of preparation is as follows:—

1. *Quiniodol* 5 per cent.
   - *a.* Dissolve 5 gr. of iodine in 100 c.c. of ether.
   - *b.* Add 100 gr. of powdered red cinchona.
   - *c.* Triturate the mass until the ether has evaporated completely.
   - *d.* Pass the powder so obtained through a fine sieve.
2. *Quiniodol* 10 per cent.
   10 gr. of iodine are dissolved in 200 c.c. of ether and triturated with 100 gr. of powdered cinchona.

The 10 per cent. strength is used for gangrenous wounds, the 5 per cent. for sluggish and slightly infected wounds.—(*Paris médical.*)

TREATMENT OF TONSILLITIS.

Lapat deals with tonsillitis as a local infection in the first few hours, and uses applications to destroy the bacilli and their toxins. He has found hydrogen peroxide and a solution of iodine, 5 per cent. stronger than the tincture, the best for the purpose. He removes the exudation from the tonsils by swabbing with hydrogen peroxide and then on another swab applies iodine to the crypts. These applications are made twice a day, care being taken that no iodine runs down into the pharynx. The throat is sprayed as well with

℞ Ichthyolis - - - - - ʒii.
Olei Anisi - - - - - ♏iii.
Aquam Anisi - - - - ad ʒii.

Misce.

"To be used as a spray every two hours."

(*Medical Record*, August 14.)

TREATMENT OF WARTS.

According to Rosenberg, cinnamon oil is an excellent remedy for warts. A drop of the oil is applied every day to each wart, and their disappearance follows in a few days leaving no scars. Neither pain nor burning is caused by the application.—(*American Medicine*, February, 1915.)

TREATMENT OF ACUTE PROSTATITIS.

Robinson adopts the following line of treatment. The patient is sent to bed, and all local treatment of the urethra is stopped. Internal treatment, however, should be continued, especially with sandal-wood oil preparations, for these relieve the dysuria, make the urine unirritating, and apparently have a good effect upon the prostate. Magnesium sulphate is

given in doses of 1 to 2 drachms four times a day. This prevents constipation, and has a useful effect on the fever and toxæmia. If the temperature is over 102° and there is severe headache, Robinson gives one or more doses of acetyl-salicylic acid, phenazone, phenacetin, or pyramidon. These not only bring down the temperature and relieve the headache, but lessen the pain in the prostate as well.

In the case of severe pain in the prostate, causing loss of sleep, Robinson prefers to give a suppository composed of:—

℞ Morphinæ Sulphatis
Extracti Belladonnæ - - - - ana gr. $\frac{1}{3}$
Olei Theobromatis - - - - - gr. xx.
Misce. Fiat suppositorium.

Hot douches in the rectum have a useful effect, especially if suppuration has begun in the gland. They may consist of 6 ounces of hot water, containing 10 minims of laudanum and 10 grains of phenazone. A useful suppository contains:—

℞ Iodoformi - - - - - - gr. ij.
Phenazoni - - - - - - gr. v.
Morphinæ Sulphatis - - - - gr. $\frac{1}{4}$.
Olei Theobromatis - - - - - q.s.
Misce. Fiat suppositorium.

"One to be introduced three times a day."

Massage should be used only in the chronic stage of the disease, never in the acute. If pus is expressed into the urethra by the massage, the urethra must be washed out gently with $\frac{1}{4000}$ solution of permanganate of potash or $\frac{1}{1000}$ of silver nitrate.—(*Amer. Jour. of Clin. Med.*, December, 1914.)

TREATMENT OF DIPHTHERIA CARRIERS.

Miller recommends spraying the throat with a solution varying in strength from $\frac{1}{4}$ to 1 per cent. of the 40 per cent. formaldehyde solution. The spraying should be carried out one hour before or not less than two hours after taking food or drink, and repeated every three or four through the day. The solution should be used quite warm and must be prepared freshly each day. It is advisable to begin with $\frac{1}{4}$ per cent. strength and to increase gradually. From three to six days' treatment is required, and the urine must be tested daily to see if any effect is produced on the kidneys.—(*Medical Record*, July 25, 1914.)

Reviews of Books.

Medical Diagnosis. By Arthur Latham, M.A., M.D., F.R.C.P., and James Torrens, M.B., B.S., M.R.C.P. Pp. 641. With 74 illustrations, 19 in colour. London: J. and A. Churchill. 15s. net.

With Macbeth we may exclaim, "The cry is still 'They come,'" for this is the fourth work on medical diagnosis we have been called upon to review within the last eighteen months. The book before us, however, differs notably from those we have previously reviewed. It really amounts to a system of medicine, with the exclusion of ætiology and treatment. Take, for example, the article on Lobar Pneumonia; under this we have the following headings: Definitions, Bacteriology, Incubation Period, Course, Physical Signs in the Chest, Varieties, Complications, Diagnosis, and Differential Diagnosis. It seems almost a pity that when so much is given that the work is not rendered complete by adding a section on Treatment and other smaller points which have been omitted. If this had been done, we should have had an excellent work on Medicine quite up to date.

The bacteriological and other tests are so fully and clearly described that the novice should be able to understand, and after some practice to carry out, the various methods recommended. We are particularly struck by the table on the more common cases of splenic enlargement and the means of diagnosis between them. We would now draw attention to a few blemishes. Among the varieties of typhoid fever, no mention is made of the form in which the larynx is primarily affected—the laryngo-typhus of continental writers. "Osteocopic pains," the letter "s" has evidently dropped out. The authors write "hoarseness or loss of voice from abductor paralysis of the left vocal cord." This is not in accord with our experience; until there is complete paralysis of the left recurrent nerve the voice is but little, if at all, affected. Melæna is mentioned as being common in duodenal ulcer, but no stress is laid upon its diagnostic value. In a work on diagnosis, chloroma should certainly receive some attention. The clinical features of lymphadenoma are described, but the chronic recurrent fever which is such a characteristic symptom of some cases is not mentioned.

The illustrations, especially those of the examinations of the blood, deserve the highest commendation, and will be found of great assistance to the student. The index might be improved, *e.g.*, on looking up "Temperature," the only reference given is relapsing fever, surely in many other diseases the temperature is equally important. Melæna is not indexed, and so on.

However, as we said before, the special part of the work, namely, that devoted to tests and bacteriological examination is admirably done, so that we can highly commend the book.

The Alimentary Tract: A Radiographic Study. By Alfred E. Barclay, M.A., M.D., B.C., M.R.C.S., L.R.C.P. Pp. 195. London: Sherratt and Hughes. 15s. net.

This book is virtually the second edition of "The Stomach and Œsophagus"—the author's thesis for the Cambridge M.D. degree. The thesis still forms the groundwork of the present book. After four introductory pages and two chapters devoted to technique, the author proceeds to deal, in turn, with the œsophagus, the stomach (both normal and pathological), the small intestine, and the large intestine. The last 50 pages are taken up with tabulated lists of cases, bibliography, and index.

A great merit of the book is its personal character, narrating the author's own experience and observations, although he has not failed to refer to the work of others to strengthen his own contentions, or fill in gaps in his own observations. Throughout there is evidence of the earnest worker, striving to reach the light, probably spending a part of the night arranging in his mind the facts observed during the day. In some respects this process is still incomplete, as the author explains in his preface, written soon after the outbreak of the war:—"Barbarity and brute passion are let loose, armed with the gifts of applied science. Science has forged the weapons that are being turned against her. . . . It is in despondency that I pen these last lines. . . . In the shadow of this calamity I have thought it best to send out this work as it stands. Several chapters I had intended to re-write and enlarge." One is inclined to regret that Dr. Barclay did not carry out this intention, even though it involved postponing publication; but this would have meant a long delay, for Dr. Barclay is wearing the King's uniform and doing yeoman service for the wounded that fill the many hospitals of Manchester.

The functions of the several parts of the alimentary tract are described accurately and well, so that a clear picture can be formed, even by those who have not themselves studied the X-ray appearances. Not content with a mere record of observations, the author makes a determined effort to co-ordinate them, and to work out the mode of interaction of the different parts. This fact has become so firmly impressed upon him that he states it, in different words, in several parts of the book:—"Three years ago, one still clung to the original conception of the alimentary canal divided into its anatomical subdivisions. One thought of a gastric ulcer, an hour-glass stomach, a spasmodic hour-glass stomach, a duodenal ulcer, etc., as definite clinical entities. . . . One was gradually driven to the conclusion that this view was wrong, and that the diseases in the stomach and duodenum are, more often than not, end results only. . . . I am convinced that the large majority of the ulcerations met with in the stomach and duodenum are secondary manifestations, and are the direct result of disease in other parts." "The importance of examining the whole alimentary tract in every case cannot be too strongly insisted upon." These views are sound, and the author gives definite instances of the interaction of the several parts: the stomach and the duodenum; the terminal ileum on the duodenum and the stomach. In endeavouring to explain the mode of these interactions he has fixed his mind on possible nervous mechanisms of a complex kind, whereas a simple mechanical explanation is at hand in

the facts—now well known—of chronic intestinal stasis. It is curious to note that in many parts of the book the author is on the threshold of "stasis," but he never enters the portal! "In certain cases the emptying of the stomach ceases, the peristalsis quietens down, and there appears to be delay in emptying. This always seems to occur when there is a heavy collection behind the ileo-cæcal valve. One sees this sequence of events so often in this class of case that there can be no doubt as to the interpretation, *i.e.*, an ileo-pyloric reflex, yet one more of these alimentary canal reflexes that make the symptomatology of disease within the abdomen so very complex and elusive." "It looks as if the duodenum is, as it were, the central office for controlling the distribution from the stomach, and is in direct communication with all the lower alimentary tract by a complex nervous mechanism of which we, as yet, know next to nothing." All these facts, accurately observed and recorded by the author, may be explained quite simply by the facts of "stasis," and there is no need to invoke a "complex nervous mechanism." Perhaps the following vague sentence gives the best idea of the frame of mind engendered by the elusive search after complex nervous mechanisms:—"My impression is that the majority of duodenal ulcers are due to trophic changes of a reflex nature and dependent in most instances on deferred stimuli arising from lesions or toxæmias of lower parts of the alimentary tract." Then follows a more lucid sentence:—"The most fruitful source of such stimuli is probably in the terminal ileum and often dependent on the appendix in some way."

Several casual phrases show that the author's mind is not conversant with the "stasis" point of view. "Lane's kink I have not recognised radiographically, and I am far from convinced that it is a cause of ileal stasis." "Ileal stasis is, up to a certain point, a physiological condition." This, of course, is a contradiction of terms, since the word "stasis" implies an *undue* delay. Many of the facts of stasis are described quite correctly; for instance, the author notices that in cases of duodenal "irritation" or ulcer there is in each case "quite well-defined ileal stasis." He adds: "These observations give the impression that the terminal ileum is abnormal in some way." The chief stumbling-block in the way of his accepting the teaching of "stasis" seems to be his conviction that the "Great Architect" would not have given man a large intestine, if it were useless to him. One is surprised to see this argument in a serious medical treatise, seeing that it would apply equally to the appendix, or indeed to disease in general. We look forward to the evolution of the author's views on these matters; meanwhile we recommend the book to those interested in the study of the alimentary tract, no matter from what standpoint. The book is printed on good paper in clear type, and there are 77 excellent figures, principally skiagrams, well reproduced on special art plates.

The Diagnosis and the Treatment of Digestive Diseases, a Practical Treatise for Students and Practitioners of Medicine. By GEORGE M. NILES. M.D. Pp. 597. With 1 coloured plate and 86 other illustrations. London: Henry Kimpton. 21s. net.

IN his preface, the author says that he has endeavoured to meet the requirements not only of general practitioners but also of specialists in

other lines, who "need a compact book which shall contain, first, concise, but easily intelligible, descriptions of the various reliable tests for the objects of study in the gastric contents, intestinal juices, and fæces; second, practicable and least disturbing methods of determining the position, size, motility, etc., of the stomach, intestines, and other abdominal viscera; third, a succinct statement of the diagnostic methods indicated in the recognition of digestive diseases; and finally, an exhaustive discussion of both general and special therapy as applied to these diseases." The above is an accurate account of the object and scope of the book under consideration, and from a careful perusal of it we can agree that the author has succeeded in his attempt.

The chapter devoted to the consideration of the conditions requiring surgical interference is an excellent one, and it contains some illuminating cases. There are, we take it, not many surgeons who would agree with the following statement in regard to appendicitis: "Let me affirm that but few cases, unless they be of the fulminating type, require operative interference during the first attack." The author, however, goes on to mention some of the conditions in a first attack in which an operation is urgently indicated.

The chapter on hydrotherapy gives a good account of the use of water in gastro-intestinal diseases. The author is strongly opposed to the limitation of fluids at meal times, and he believes that the presence of an abundance of water during the busy period of digestion is very desirable. One of the most remarkable features of the book is its hopefulness. The author is a firm believer in the virtue of psychotherapy, and he is constantly inculcating the necessity of infusing courage and cheer into the mind of the invalid.

The author seems rather doubtful as to the spelling of a distinguished English surgeon's name, as on one page he has Moyihan and Myonihan. We do not think that "internist," meaning a physician who devotes himself to abdominal affections, is a desirable addition to the English language, though from the author's use of it, it seems current in America. We can thoroughly recommend the book as a modern and reliable work on the disorders of digestion, and a credit to American medicine.

Medical and Pharmaceutical Latin for Students of Medicine and Pharmacy. By Reginald R. Bennett, B.Sc., F.I.C. Pp. xiv. + 443. Second edition. London: J. and A. Churchill. 6s. 6d. net.

This is the modern *Selecta é Prescriptis*, of which Dr. Jonathan Pereira published the first edition in 1824, when he was about twenty years of age, It is hardly necessary to say that Mr. Bennett has found it desirable to incorporate a great deal more matter dealing with Latin grammar than appeared requisite eighty years ago. The work in its present form has been before the medical profession for about eight years, and has come to be regarded as the best text-book on the subject of prescription-writing from the linguistic point of view. It is well arranged, well printed, and contains such an admirable collection of typical prescriptions as to meet every requirement of the student of medicine. This second edition has

been improved in respect of some of the older formulæ being replaced by some modern ones, and the vocabularies have been enlarged.

Gonorrhœa and its Complications in the Male and Female. By David Watson. M.B., C.M. Pp. 375. London: Henry Kimpton. 15s. net.

Books on gonorrhœa are not legion, so it is with pleasure that we have read through the one we have before us. The chapter on bacteriology would have been better, if it contained only those methods of staining the gonococcus which the author had himself found useful. It appears to us to be a mistake to load books with various methods of staining, of treatment, etc., of which the author has had no personal experience. After all, most of them have only seen daylight, because someone wishes to do something different from someone else, and trusts that the method will be called after his name.

The chapters on uncomplicated gonorrhœa, as it affects the male and female, are very good, but we are surprised to find that the author is a strong advocate of treatment by means of the urethroscope. We have seen too many of the supposed cures in Germany to believe that the urethroscope can be of service other than to diagnose the site of the mischief. We note that the author thinks that the presence of gonococci in the polymorphonuclear leucocytes indicates that phagocytosis has taken place. Considering how well they flourish, would it not be more reasonable to expect that the organisms are living at the expense of the leucocytes? A little more attention to the abortive treatment might be given. The chapters on gonococcal complications are, considering the scope of the book, not dealt with fully enough. For instance, we are surprised to find no mention of gonococcal neuritis. The chapter on immunity reactions could certainly be amplified.

There are a few misprints which could be corrected, should another edition come out—*vide* pages 265 and 293, "colossal" instead of "collosol." Should the author think of bringing out another edition, he might omit the coloured plates, which are not good, and reduce the price of the book, for the number of readers who are prepared to give 15s. for a book on gonorrhœa must be very few.

Operative Surgery. The Head and Neck: The Thorax and Abdomen. By Edward H. Taylor, M.D., B.S., F.R.C.S.I. Illustrated. Pp. 505. London: J. and A. Churchill. 30s. net.

The author of this excellent book remarks in his preface that this treatise differs from the ordinary works on the subject in several respects, and that he has heard a wish expressed for a work of the kind. This is indeed true, and he has throughout kept this before his mind in describing with extraordinary skill, the minutiæ of operative manipulation.

There are many young surgeons who feel handicapped for the want of some work giving a clear description of these details, and though they are constantly witnessed when watching an operation skilfully performed, they are apt to pass almost unnoticed, unless special attention is directed to them, when all is plain sailing and no difficulties calling for unusual treatment occur. In this book, attention is called to these points, and great value lies therein; for unless the young operator is aware of the pitfalls he is likely to encounter, and is alive to the best and usual methods of dealing with

them, he will have to invent for himself, on the spur of the moment, some satisfactory means of escape, which is not always easy and is often unnerving. Those who realize these facts, and have perhaps some misgivings, may safely and with complete confidence study this work, and will find not only a perfect description of most of the typical operations likely to come into the scope of the general surgeon, but innumerable tips and suggestions how to circumvent likely difficulties; subsequently, under the title of "Comments," special attention is called to practical difficulties and their treatment.

The author has chosen good sound methods, not, as a rule, attempting to give all the alternative methods invented; this we believe valuable to those for whom the book is written, in that it aims at accurately mastering the best, or one of the best, procedures, in place of obtaining a more vague idea of several.

The drawings are admirable, accurate, most helpful, and quite among the best yet published. The chapter on surgical technique and anæsthetics is valuable.

All the subjects dealt with are so excellent, that it is difficult to award laurels to any; but perhaps especial appreciation may be directed to those dealing with the thyroid, larynx, hernia, gastro-intestinal, and renal operations. The section describing removal of malignant diseases of the colon is the best on the subject we have read.

The type is large and clear, and the index is complete and good.

The whole work fulfils its purpose in every way, and reflects the highest credit upon all concerned in its production. We hope to see another volume treating of other branches of operative surgery by the same skilful pen.

Errors and Missprints detected.—Page 238, line 8, "should"; page 328, line 25, *insert words* "the junction of" *between* "level of . . . the middle with"; page 403, bottom line, "absorbable"; page 448, line 7, "pyelomphritis"; page 465, line 5 from bottom, "intestine"; page 489, line 7, "useful."

Minor Surgery and Bandaging. Pollard. By H. Morriston Davies, M.D., M.C., F.R.C.S. Pp. 467. London: J. and A. Churchill. 7s. 6d. net.

The fact that this work has now reached the 15th edition is sufficient evidence of the excellence of its predecessors. The present edition has been considerably improved. The chapter on "Poisons and their Antidotes" has been omitted. It is perhaps rather on the side of loss than of gain that this subject is not mentioned, for although this class of case is not usually treated by the surgeon, it is one which may not infrequently come under his notice, especially in the casualty rooms of our larger hospitals.

The chapter on "the Examination of the Patient" (Chapter 1) is very good; every example and suggestion given is of the utmost importance, and of great practical use. The descriptions of the additional operations—those for hernia, varicocele, etc., are clear and lucid, and will be found extremely valuable to the house-surgeon, to whom more and more of these operations are now entrusted. There are nearly 100 new illustrations in the book, all of which are excellent.

The 15th edition has, if possible, surpassed in usefulness the former ones, and the work still remains the best of its kind now in print. It can be recommended with the utmost confidence to be a great help to house-surgeons and practitioners alike.

Surgery: Its Principles and Practice. By A. P. C. Ashurst, M.D., F.R.C.S. Pp. 1141. London: Henry Kimpton. 28s. net.

The object of the book, as described by the author, is first to give the student a foundation on which to build a knowledge of surgery, and secondly, to present to the practitioner a book of reference. The references are not given in the usual form of a bibliography, but the names of the authors and the dates of publication of their works are given in the text.

The book is divided into three sections:—General Surgery, Systemic Surgery, and Regional Surgery. It contains 7 coloured plates, all of which are excellent, and 1032 illustrations in the text. The latter are on the whole good, except that it is unfortunate that in the present state of aseptic surgery, a surgeon should be depicted performing the operation of circumcision with a ring on his finger (p. 1047).

The section on General Surgery, though of necessity somewhat curtailed, is good. The section on Systemic Surgery, especially those chapters dealing with fractures and orthopœdic surgery, is excellent, the illustrations are good, and the indications for, and the methods of, treatment are clear and concise.

In the section on Regional Surgery, the chapters given to diseases of the breast and diseases of the genito-urinary system are the best; the treatment is shortly but well indicated, and the details of operations sufficiently clear and up to date. The chapter on the stomach and duodenum is disappointing, and in places inaccurate. The symptoms of gastric and duodenal ulcer are considered under one heading, and no effort is made towards a differential diagnosis between the two. The symptoms of gastric and duodenal ulcer, according to those in a position to speak with authority, are entirely different, and the diagnosis, especially of the latter, a matter of certainty in a very large majority of cases. "Hunger-pain," a pathognomonic symptom of duodenal ulcer, is associated in the text with the name of Mayo Robson, although this symptom was first described and the term invented by Moynihan. When enumerating the symptoms of perforated gastric or duodenal ulcer, the author says, "the patient may be found rolling around in agony." This is not in accord with the general teaching, as a patient with a perforation remains absolutely still and dare not move in the slightest degree. The pulse is said to be either rapid or slow. The pulse is never rapid at the time of perforation, and does not become so until peritonitis is progressing. This slow pulse may therefore, if not recognized, lead to the waste of valuable time, and is an extremely important point to emphasize. It is doubtful, too, if many surgeons will agree with the statement that in perforations, in "all cases the pelvis should be drained . . . as well as the upper abdominal wound."

With the exception, perhaps, of the chapters on stomach and duodenum, the book may be recommended to "furnish the foundation on which a knowledge of surgery is to be built."

Preparations, Inventions, etc.

"GRANSALO FOOD."

(Edinburgh: Messrs. Simon Henderson and Sons, Slateford Road.)

This new preparation consists chiefly of flour and eggs baked by a special process which breaks up the starch granules and makes them soluble to a large extent. It has been analysed by Dr. Drinkwater, who reports the following results:—

Moisture	8·02		
Albuminoids	15·75 = Nitrogen	2·52	per cent.
Fat	10·80		
Carbohydrates	64·64 = Soluble	18·63	per cent.
Ash	0·81 = P_2O_5	0·383	per cent.
Fibre	0·08		
	100·10		

The phosphorus is present partly in the form of lecithin. The preparation is a light fawn-coloured powder, with a pleasant aroma, and mixes well with hot water, milk, or cream, forming a delicately flavoured beverage.

Its constitution and solubility bear out the claim made for it as being well suited for nursing mothers, infants over six months old, invalids, and people with weak digestion. It has been submitted to extensive trials with excellent results, and is fully entitled to be considered as a valuable addition to the dietary for the special purposes mentioned.

"WANDER" MALT EXTRACT WITH PARAFFIN.

(London: Messrs. A. Wander, Ltd., 45, Cowcross Street, E.C.)

In this new preparation, the crystalline "Wander" malt extract is combined with equal parts of pure liquid paraffin. It is very palatable, and can be taken dry from a spoon, or mixed with water or milk without appreciable separation of the oily constituent. It is, therefore, specially suitable for children, as well as for those who cannot tolerate any oily preparation. The slightly laxative properties of the malt extract tends to increase the effect of the paraffin. The "dry emulsion" form ensures that the paraffin mixes thoroughly with the contents of the bowel, thus preventing the formation of scybala, while at the same time the mechanical action of paraffin on the bowel wall is materially assisted. It is suitable for use in all conditions for which liquid paraffin is taken.

SEDOBROL.

(London: The Hoffmann-La Roche Chemical Works, Ltd., Idol Lane, E.C.)

This dietetic bromide product was reported upon in these notes a short time ago. Messrs. Hoffmann-La Roche have now issued, and will be pleased to send a copy post free on application, a reprint of a recent paper read by Dr. Ulrich, the Medical Superintendent of the Swiss Institute for Epileptics in Zurich, entitled "Notes on the Technique of Effective Bromide Therapy in Epilepsy." The paper is based upon the experience gained from the treatment of several hundred epileptics by this combination of bromine and

a diet restricted in salt.

PROTARGEN.

(London: Mellin's Pharmacy, 48, Regent Street, Piccadilly Circus, W.)

This new product is an albuminate of silver, and is a fine powder, pale yellow in colour, and readily soluble in water. The solution does not coagulate on boiling, and no precipitate is given with albumen, dilute hydrochloric acid, solutions of sodium chloride, potassium chromate, or any of the reagents for silver. The solution possesses well marked colloid properties. These, together with its perfect solubility and its non-precipitation with albumen and salt, enable it to bring its full activity into play in the presence of the body fluids, and to penetrate deeply into the mucous membranes. It is, consequently, quite free from all corrosive, irritating, or staining effects, and can be used with good results in all cases in which nitrate of silver is indicated, either as injection, lotion, or ointment. Its free solubility allows lotions to be made of any strength from 0·25 per cent. to 25 per cent.

It is produced entirely in this country to take the place of similar compounds previously imported from Germany and Austria; and, so far as we have been able to test, it is fully equal to these in therapeutic properties.

A SELF-RETAINING BLADDER RETRACTOR.

(London: Messrs. Allen and Hanburys, Ltd., 48, Wigmore Street, W.)

The efficient exposure of the interior of the bladder is the key-note to modern operations on that viscus. Some years ago Mr. Thomson Walker introduced a bladder retractor with an easily grasped handle, which gave a maximum exposure of the interior of the bladder, for the size of the

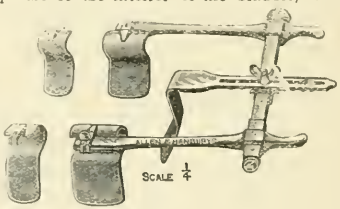

Fig. 1.

abdominal incision. In order to diminish the amount of assistance required at operations on bladder growths he has had the blades of the bladder retractor fitted on an abdominal frame, so that they can be slipped into the cavity of the bladder, separated, and remain in place, retracting the abdominal wall and holding the lateral walls of the bladder well apart. The blades are detachable; so that a small size or a large size blade may be used, as the exigencies of the operation demand. A third blade is attached by means of a screw to the transverse base of the frame. It is movable in an antero-posterior direction, and serves to push back the posterior wall of the bladder.

This instrument has been in use for two years, and has proved a highly efficient self-retaining bladder retractor.

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